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EFFICACY OF SUCRALFATE IN ALLEVIATION OF POSTOPERATIVE MORBIDITY AFTER TONSILLECTOMY.

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ABSTRACT… Objectives: Despite of the therapeutic advancement, post-tonsillectomy pain is one of the most commonly observed morbidities associated with this surgical procedure which in turn highlights the need for appropriate analgesic consumption that assures safety and efficacy. Through this study our basic motive was to evaluate the sucralfate efficacy in the management of post-tonsillectomy symptoms during the first week of the surgery. **Study Design:** An Interventional, Quasi Experimental, (double-blind), purposive study. **Setting:** Department of Otorhinolaryngology and Head and Neck Surgery, Dow University of Health Sciences & Civil Hospital Karachi. **Period:** From January to June 2018. **Material & Methods:** One hundred and forty tonsillectomy patients of both genders between the age group of 7 to 35 years were randomly included in the study and categorized into 2 groups i.e. trial (Sucralfate group; Group A) and control (Pyodine group; Group B) with 70 patients in each group. The patients in group A were recommended to gargle with sucralfate suspension 4 times a day while following the same procedure except the group B interventional product was replaced with Pyodine mouth wash. The post-operative symptoms and secondary outcomes including pain, otalgia, odynophagia, analgesic requirements, slough shedding, bleeding and other associated side-effects were monitored. Pain, otalgia and odynophagia were assessed using the universal pain assessment tool (UPAT) while the secondary outcomes through a scoring system generated internally. **Results:** It is revealed from the study results that there was significant decrease in the throat pain and odynophagia in group A from 3rd to 7th post-tonsillectomy day ($p < 0.05$); while the results were not very significant for otalgia. The same could be applied for other secondary outcomes i.e. the analgesic requirement greatly decreased in patients given sucralfate presenting faster recovery. Moreover, early return to normal diet was observed for the patients treated with sucralfate. No serious adverse effects observed among the patients both groups. **Conclusion:** Sucralfate can be recommended as the first choice of treatment for the management of post-tonsillectomy symptoms on the basis of its efficiency in treating pain and other symptoms and hence providing maximum safety.

Key words: Morbidity, Postoperative Pain, Sucralfate, Tonsillectomy, Universal Pain Assessment Tool (UPAT).

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INTRODUCTION

Among various otorhinolaryngologic surgeries, Tonsillectomy is the most frequently performed operative treatment.[1] During the procedure complete tonsil is removed along with its capsule[1]. It is evident that tonsillectomy alleviate acute attacks of recurrent tonsillitis, reduces airway resistance of upper respiratory tract, relieves obstructive sleep apnea, reduces intermittent pharyngitis incidences and results in improved quality of life.[2] Numerous advanced surgical interventions have now been introduced to the scientific world in order to improve the morbidity of adenotonsillectomy, cold dissection, laser tonsillectomy, ligature tonsillectomy, and hormonic tonsillectomy are few of them.[3] Bipolar diathermy is another routinely used method for tonsillectomy, an intervention that utilizes direct heat for cutting and coagulating soft tissues.[4] It is considered as the less traumatic method with quicker recovery.[4] With these advanced techniques the surgeons have overcome the

problem of post-tonsillectomy pain up to some extent but it is still a point of concern after the procedure. Hence new methods are still under consideration for complete and rapid pain recovery.

The inflammation of nerve endings and spasm of the pharyngeal muscles leads to Post-tonsillectomy pain.[2] These pain sensations are strongest during the first few days after the surgery leading to reduced dietary intake and hence causing dehydration.[2] It lasts unless a mucous membrane re-develops over the inflamed muscles.[5] Post-operative management and supervision is necessary to ensure pain recovery, nutritional and swallowing improvements so that the patients pursue normal daily activities as early as possible.[6] It is evident that utilization of more than one analgesic is universally accepted fact in case of Post-operative pain of tonsillectomy.[7] Different topical solutions are being used during post-operative period, usually paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) are used in combination.[1] However, the adverse effects caused by NSAIDs on the platelet function cannot be neglected as it is the core reason behind postoperative bleeding among tonsillectomy patients.[1]

The sucralfate topical suspension for the treatment of tonsillectomy pain is trending in the surgical world and is associated with astonishing pain relief. It is a polyaluminum hydroxide complex salt with a sulfated disaccharide skeleton, widely used for the treatment of peptic ulcer.[6] It effectively provides protective barrier, reduces the morbidity and aids in early wound healing, leads to faster recovery by coating the tonsillar bed after Tonsillectomy.[5] It is responsible for tonsillar regeneration by forming polyvalent bridges between the negatively charged polyanion and positively charged constituents in mucosal lesions mainly the mucosal proteins.[8] Sucralfate, being a strong antiulcer agent also acts as acid buffer, depletes gastric acids and pepsin.[8]

In addition to the regeneration and production of mucous membrane, sucralfate also supports migration of the cells, mitotic activity, promotes prostaglandin E2 production and thus increasing the blood flow.[9] It stimulates the production of growth factors mainly fibroblast growth factor leading to rapid healing of epithelial wounds (angiogenesis).[9] The drug efficiency is proven worldwide as it mainly acts on the site of ulcer and holds minimal side-effects.[9] No serious side-effects are associated with Sucralfate use according to previous literature while constipation is the most commonly reported minor side-effect.[10] Through this study our aim was to evaluate the efficacy of sucralfate in the reduction of symptoms associated with tonsillectomy and the duration and trends in recovery during the first 7 postoperative days.

METHODOLOGY

Study Design & Setting

This Interventional, Quasi Experimental, (double-blind), purposive study was conducted at the Department of Otorhinolaryngology and Head and Neck Surgery, Dow University Of Health Sciences & Civil Hospital Karachi. The study continued for 6 months from January to June 2018 in accordance to the ICH-GCP guidelines (International Conference on Harmonization - Good Clinical Practice) and the ethical approval was received from AEIRC Committee on Ethics (Ref. No. MO/EMA/58/709) prior to the study. Informed consent was received from each patient enrolled in the study.

Patients

A total of 140 Post-Tonsillectomy patients between the age group of 7 to 35 years (with a mean age of 14.81 $\pm$7.35 years) irrespective of gender were included in the study. These patients were divided into two groups' trial (Group A) and control (Group B) with 70 patients in each. The tonsillectomy was performed by cold steel dissection method under the supervision of senior ENT surgeon.

Drug Administration

Sucralfate suspension was administered for the patients of trial group. The patients were recommended to gargle with 10-15ml of the given suspension for 4 times a day for approximately 5 minutes. For the patients in control group

sucralfate suspension was replaced with Pyodine mouth wash while keeping the frequency and intervals similar to that of the comparative group.

Methods

The patients were assessed for symptoms of Post-Tonsillectomy including pain, otalgia, odynophagia and bleeding. The assessment continued for a period of 7 post-operative days, Universal Pain Assessment Tool (UPAT) was utilized for the assessment of pain, otalgia and odynophagia. The analgesic requirement and post-operative dietary routine were also recorded in the individual follow-up diary through numerical scoring system developed internally.

Analgesic Requirement	Scores
No Analgesics Required	0
Once Daily	2
Twice Daily	4
Thrice daily	6
Additional Analgesics	8
Post-Operative Dietary Routine	
After Day 7	0
Day 7	2
Day 5	4
Slough shedding	
After Day 7	0
Day 7	2
Day 5	4

Scoring system for secondary outcomes

Statistical Analysis

Data was analyzed through Statistical Package for the Social Sciences (SPSS) version 22. Data with regards to pain, otalgia, odynophagia, analgesic requirement, dietary intake and slough shedding was presented as frequency and percentages. Non-parametric tests i.e. Mann-Whitney U test was used to find the differences between the trial and control group. P value< 0.05 was considered significant.

RESULTS

In this study, 70 post-tonsillectomy patients were randomly assigned to trial (Group A) and control group (Group B). The mean age of the study subjects was 15.24 $\pm$7.23 years in trial group while 14.38 $\pm$7.50 years in the control group. There were 35 males and 35 females in group A whereas 36 males and 34 females in group B.

Primary Outcomes

According to the results the post-operative patients administered sucralfate i.e. trial group experienced much quicker soothing effect as compared to the control group during the period of day 3 to day 7 after tonsillectomy ($p<0.05$). Statistically significant decrease in the throat pain was observed in both groups on post-tonsillectomy day 7 (Table-I).

Unlike throat pain the results for Otalgia were comparatively insignificant for day 3 and day 7 ($p>0.05$) while a significant decline can only be observed for day 5 after tonsillectomy. Hence it can be noted that 38 patients from group A while only 22 patients from group B reported no pain on day 5 ($p<0.05$). Table-II

By the end of the first pre-operative week mild odynophagia was observed in 37.1% of the patients from group A and 42.9% from group B. None of the cases with severe odynophagia were reported by the post-tonsillectomy day 7. Moreover a significant decrease in Odynophagia was observed in both groups from day 3 to day 7 ($p<0.05$). Table-III

Secondary Outcomes

As shown in Table-IV, by the end of the first post-tonsillectomy week patients from group A, barely needed additional analgesics while 16 from group B were dependent upon additional analgesic by the end of the week. The requirement for analgesic significantly reduced from day 3 to day 7 among both trial and control group patients ($p<0.05$).

A significant progress was observed in the patients of both group ($p<0.05$) although routine dietary intake in the progression was quite rapid among the sucralfate patients i.e. trial group in comparison to those in control group. The regaining process being slow in group B, 28/70 from group A while none from group B returned to normal dietary intake on day 5 of tonsillectomy. Table-V

Significant difference in slough shedding was

observed among patients of both groups ($p<0.05$). After 7th day of tonsillectomy slough was observed in only 3 patients from group A while among 34 patients from group B. No episodes of bleeding was observed in any of the patients of the two groups. Table-VI

			Pain					
			Mild	**Moderate**	**Severe**	**Very Severe**	**Worst Possible Pain**	**P-Value**
Day 3	Group A	n	17	38	15	0	0	0.001*
		%	24.3	54.3	21.4	0.0	0.0	
	Group B	n	0	49	16	3	2	
		%	0.0	70.0	22.9	4.3	2.9	
Day 5	Group A	n	41	25	4			0.078
		%	58.6	35.7	5.7	-	-	
	Group B	n	33	25	12			
		%	47.1	35.7	17.1	-	-	
Day 7	Group A	n	29	34	7			0.006*
		%	41.4	48.6	10.0	-	-	
	Group B	n	16	38	16	-	-	
		%	22.9	54.3	22.9	-	-	

*Group A= Trial Group; Group B= Control Group; UPAT= Universal Pain Assessment Tool
*p-value calculated using Mann-Whitney U Test.

Table-I. Throat pain in Group A and Group B on day 3, 5 and 7 on the basis of UPAT scores

			Otalgia			
			No Pain	**Mild**	**Moderate**	**P-Value**
Day 3	Group A	n	46	22	2	0.257
		%	65.7	31.4	2.9	
	Group B	n	42	18	10	
		%	60.0	25.7	14.3	
Day 5	Group A	n	38	27	5	0.009*
		%	54.3	38.6	7.1	
	Group B	n	22	40	8	
		%	31.4	57.1	11.4	
Day 7	Group A	n	65	4	1	0.186
		%	92.9	5.	1.4	
	Group B	n	60	10	0	
		%	85.7	14.3	0.0	

*Group A= Trial Group; Group B= Control Group; UPAT= Universal Pain Assessment Tool
*p-value calculated using Mann-Whitney U Test.

Table-II. Otalgia in Group A and Group B on day 3, 5 and 7 on the basis of UPAT scores

			Odynophagia					
			No Pain	**Mild**	**Moderate**	**Severe**	**Very Severe**	**P-Value**
Day 3	Group A	n	2	18	34	16	0	0.002*
		%	2.9	25.7	48.6	22.9	0.0	
	Group B	n	0	1	48	18	3	
		%	0.0	1.4	68.6	25.7	4.3	
Day 5	Group A	n	6	43	19	2	0	<0.001*
		%	8.6	61.4	27.1	2.9	0.0	
	Group B	n	1	29	26	13	1	
		%	1.4	41.4	37.1	18.6	1.4	
Day 7	Group A	n	35	26	9	-	-	0.013*
		%	50.0	37.1	12.9	-	-	
	Group B	n	22	30	18	-	-	
		%	31.4	42.9	25.7	-	-	

*Group A= Trial Group; Group B= Control Group; UPAT= Universal Pain Assessment Tool
*p-value calculated using Mann-Whitney U Test.

Table-III. Odynophagia in Group A and Group B on day 3, 5 and 7 on the basis of UPAT scores

			Analgesic Requirement				
			Once Daily	**Twice Daily**	**Thrice Daily**	**Additional Analgesic**	**P-Value**
Day 3	Group A	n	3	40	27	0	<0.001*
		%	4.3	57.1	38.6	0.0	
	Group B	n	0	20	48	2	
		%	0.0	28.6	68.6	2.9	
Day 5	Group A	n	1	31	26	12	<0.001*
		%	1.4	44.3	37.1	17.1	
	Group B	n	0	4	41	25	
		%	0.0	5.7	58.6	35.7	
Day 7	Group A	n	36	18	15	1	<0.001*
		%	51.4	25.7	21.4	1.4	
	Group B	n	11	25	18	16	
		%	15.7	35.7	25.7	22.9	

*Group A= Trial Group; Group B= Control Group; UPAT= Universal Pain Assessment Tool
*p-value calculated using Mann-Whitney U Test.

Table-IV. Comparison of analgesic requirement in trial and control group on day 3, 5 and 7 on the basis of numerical scoring system developed internally

		Dietary Intake			
		After 7th Day	**On 7th Day**	**On 5th Day**	**P-Value**
Group A	n	12	30	28	<0.001*
	%	17.1	42.9	40.0	
Group B	n	37	33	0	
	%	52.9	47.1	0.0	

*Group A= Trial Group; Group B= Control Group
*p-value calculated using Mann-Whitney U Test.

Table-V. Time taken by the patients to return to normal dietary intake in both groups

		Slough Shedding			
		After 7th Day	**On 7th Day**	**On 5th Day**	**P-Value**
Group A	n	3	31	36	<0.001*
	%	4.3	44.3	51.4	
Group B	n	34	36	0	
	%	48.6	51.4	0.0	

*Group A= Trial Group; Group B= Control Group
*p-value calculated using Mann-Whitney U Test.

Table-VI. Differential observation of Slough shedding by the week after post-tonsillectomy

DISCUSSION

Although being the treatment of choice in chronic tonsillitis and obstructive sleep apnea, Tonsillectomy is still associated with post-operative morbidities. Despite of the consistent discoveries in the field, no drug has yet been identified minimizing the side-effects entirely and providing faster and better recovery with minimum effect on the quality of life of the patients.[5] One of the emerging therapeutic preference is sucralfate, rapidly gaining trust as it has been linked to quicker recovery and reduced morbidity rate after procedure with least observed side-effects.[5,9,11,12]

Our aim was to disclose the efficacy of sucralfate among tonsillectomy patients and for this reason the prevalence of post-operative symptoms were observed in the study population and the results were also compared with the control group. Results showed that trial group patients administered sucralfate reported lesser throat pain during the first postoperative week as compared to the control group ($p < 0.05$). Inconsistent results were observed in case of otalgia while significant decline was observed in the intensity of odynophagia in both the groups with improved results in the trial group comparatively.

Similarly a study concluded that sucralfate holds profound effect in alleviation of post-operative odynophagia.[13] Likewise, another study reported decreased post-operative symptom scores among the tonsillectomy patients treated with sucralfate.[6] In contrast, Freeman and Markwell in their study observed no significant effect of sucralfate in reducing pain during the 10 post-operative days.[14] These variations may be due the differences in gender, population size, operation techniques and age group etc.

Secondary outcomes of the treatment were also investigated, significant decline in the analgesic requirement was observed in trial group treated with sucralfate as compared to the control group. Similarly Özcan and his colleagues concluded that the use of analgesics (paracetamol) is decreased from day 3 to day 7 after tonsillectomy among the patients primarily on sucralfate therapy.[15] While a few studies showed no difference in the duration of analgesic use among the patients on sucralfate.[11&12] One of the reasons for the increased severity of post-operative morbidities among adults in comparison to children is due to the complexity of the procedure among adults although their endurance is greater but due to the fact that the children despite of being in more pain do not present the urge of medication by themselves while in contrast adults do approach therapeutics for pain management.[16]

Additionally, the drug did not cause any side-effects and no bleeding was observed. This is due to the fact that absorption factor of sucralfate is very small and is observed in very few cases so the chances of side-effects are nil or rare.[10] Common reported adverse effect is constipation and in rare cases nausea, vomiting, rash, pruritus, allergies etc. might be observed.[10,16,17] Hence, the study proves the efficacy of sucralfate in reducing throat pain, otalgia and odynophagia by creating a fine protective barrier against the inflamed mucosa leading to fast recovery. Further research is required to evaluate the drug effect on quality of life of the patients and the differential variations in the primary and secondary outcomes after treatment and its association with age, gender and other associated factors.

CONCLUSION

It can be concluded from the study results that Sucralfate has enhanced tolerability and is safer to use in comparison to other drugs as it ensures minimum side-effects and brings up faster recovery. It assures the management of post-operative pain and other associated symptoms. Sucralfate can be recommended as the prime drug of choice for the post-tonsillectomy patients as it is cost-effective and aids in early retrieval of normal daily routine.

CONFLICT OF INTREST

The authors declare no conflicts of interests.

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