Comparing The Efficacy Of Various Adjuvant Therapy To Prevent The Recurrence Of Odontogenic Keratocyst: Review Of Literature.

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Abstract

Objective: Odontogenic keratocyst being a more aggressive odontogenic cyst with higher recurrence rate, proper diagnosis and treatment plays a key role in its management. The treatment plan involves enucleation with or without marsupialization followed by various adjuvant therapy such as Carnoy's solution ,Modified Carnoy's ,5 fluorouracil and various other therapies such as cryotherapy and phototherapy for destruction of the daughter cells thus preventing the recurrence.Among the above various adjuvant modalities its still not clear which is superior to the other. In this review article we compare the efficacy ,biocompatibility , recurrence rate and complications associated with Carnoy's,modified Carnoy's and 5 fluorouracil based on various literatures.

Materials and methods: This review follows PRISMA guidelines.Database was collected from Pubmed search engine for articles involving the treatment of patients diagnosed with odontogenic keratocyst, primarily treated with Enucleation with or without marsupialization followed by adjuvant therapy.Studies for a period of 10 years from 2013-2023,in English literature and full length articles were included in the study. Studies involving only primary surgical treatment without adjuvant therapy were excluded. Out of 133 articles,8. articles were included in this study based on inclusion and exclusion criteria.

Results: The mean age of the patients was 35 years and the follow-up period is 2-6 years. There was a low recurrence rate in cases where 5FU has been used as an adjuvant therapy compared to patients who underwent adjuvant therapy involving peripheral osteotomy and modified carnoy's solutions. Modified carnoy's solution shows incidence of permanent nerve paraesthesia and swelling post operatively. Peripheral osteotomy alone after enucleation shows recurrence but when combined with carnoy's solution shows less recurrence. 5FU showed lower recurrence rate and associated complications as it's an antimetabolite that targets the proliferative cells.

Conclusion: In this study we conclude that 5FU is a targeted therapy for odontogenic keratocyst when compared to other adjuvant therapies because of its minimal recurrence rate, bio-compatibility thereby reducing post-surgical morbidity. Further prospective studies using 5FU, longer follow-up times , and comparison of the use of 5FU with other effective and emerging therapies for OKCs.

Clinical relevance: This article aims to provide benefit to the clinician's to understand the efficacy of various adjuvant therapy and to diagnose and treat Odontogenic keratocyst as to minimise the complication and prevent its recurrence.

Keywords: Odontogenic keratocyst, adjuvant therapy, Carnoy's solution,5FU, Phototherapy

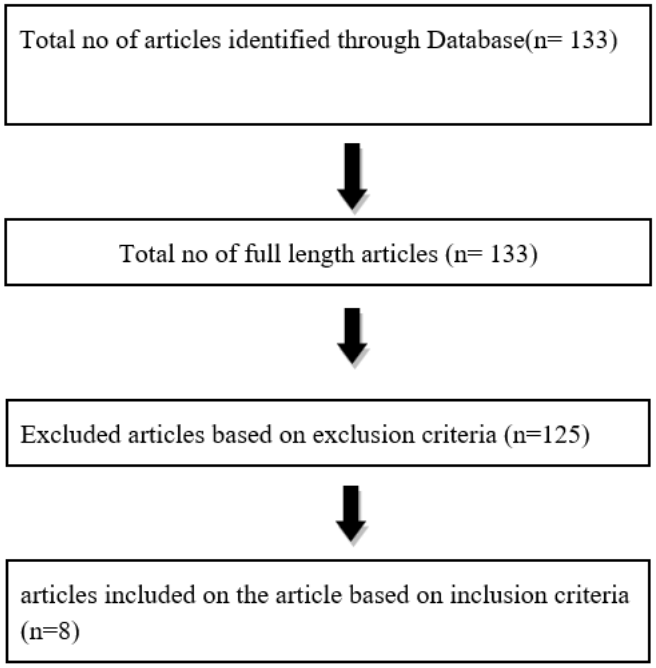
Introduction

Odontogenic keratocyst is defined as an odontogenic cyst characterized by a thin, regular lining of Para keratinized stratified squamous epithelium with palisading hyper chromatic basal cells. It is more predominantly seen in the posterior body of the mandible and arises from the remnants of dental lamina. Literature shows

the mutation of PTCH 1 gene associated with the genetic alteration involved in the occurrence of OKC. It is often associated with Nevoid basal cell carcinoma when found in other locations. The most standard definitive treatment modality being the enucleation following with or without marsupialization, the adjuvant therapy varies. In this article we compare the various adjuvant treatment methods based on their efficacy and safety. The various therapy used post enucleation of the OKC are Carnoy's solution which has the composition of 1g of ferric chloride, 6 ml of alcohol, 3 ml of chloroform ,1 ml of glacial acetic acid for application of 3 mins ,but as the chloroform has carcinogen properties, the use of Carnoy's solution had been prohibited by the US Food and Drug Administration following which the Modified Carnoy's solution was introduced with similar concentration excluding the Chloroform.5 Fluorouracil (5FU)which is an antimetabolite drug act by inhibiting the enzyme Thymidylate synthetase essential for DNA synthesis. The recurrence rate following the use of 5FU is much more similar when compared to modified Carnoy's solution stating that 5FU is equally effective compared to modified Carnoy's solution and also provides the advantage of less adverse effects on the surrounding tissues.
Peripheral osteotomy is done post enucleation where the peripheral bone surrounding the lesion is removed with powered hand piece to debride the macroscopic remnants, even though it's considered as aggressive treatment, but it has less morbidity compared to enucleation and resection. However, the literature reports that the rate of recurrence with peripheral osteotomy is 17.4 to 18.2% when compared to enucleation followed by application of Carnoy's solution which is 4.8 %to
5.3 %.

Material and methods

The systematic review was done according to the PRISMA guidelines. Data were collected from PUBMED for the period of 10 years from the year 2014-2023.Only the full-length articles in English were included in the study. Inclusion criteria was patient histologically diagnosed with Odontogenic keratocyst patients where adjuvant therapy was used following the enucleation, Exclusion criteria included were patients with any syndromes, the patient is whom only the surgical enucleation. was done as monotherapy. Data included in the checklist were the author and year of publication, study design, follow up period, location of the lesion, adjuvant therapy used recurrence rate.



RESULTS

Sl. No	Name of the author/ Year	Age(yrs) /Gender Total no: of	Site of lesion	Primary treatment done (Enucleation/marsupialization)	Adjuvant Treatment done	Follow up period	Recurrence rate/Treatment done	Complications

		cases						
1	Marco F. Caminit i [1]	71	Mandible	Enucleation and peripheral osteotomy	34 patients 5 FU & 36 patients MCS	22 Months	No recurrence in 5 FU but 9 recurrences in MCS	NIL
2	Labibah Motaleb et al[2]	56 patients 11-93 years	Mandible & maxilla	Enucleation followed by adjuvant therapy	Carnoy's solution, Cryotherapy	3 to 6 years	NIL	NIL
3	Sandip A. Wanve et al [3]	42 patients 32.81 ± 12.84 years	-----	Enucleation followed by adjuvant therapy	21 patients MCS and 41 patients 5 FU	12 months	No recurrence	Temporary paraesthesia in MCS group(n=5) with permanent paraesthesia of 4.5% and in 5FU group(n=3) with permanent paraesthesia of 0%
4	Abdul Ahad Khan et al [4]	Female 35-year- old	Mandible	Enucleation followed by the use of Carnoy's solution	Carnoy's solution	3 years	-	NIL
5	Lorenza A. Donnelly et al[5]	77 patients, 36 patients in the CS group and 41 in the MC group' median age 41.5 and 46	Posterior mandible regions	Enucleation followed by Adjuvant therapy. 36 patients in the CS group and 41 in the MC group' median age 41.5 and 46,	Carnoys and modified carnoys solution	2 years	14.29%, with 5 (13.9%) recurrences in the CS group and 6 (14.6%) in the MC group	NIL
6	Parveen Akhter Lone et al [6]	27 patients 20–66 years	posterior mandible	Enucleation followed by adjuvant therapy	Ms n=9 5FU N=11 Segmental resection n=7	Mean follow-up 3.5 years	66.6% after modified CS	nerve injury, swelling, infection, and recurrence (66.6% after modified CS) Functional and aesthetic compromise was seen in resection patients. minimal nerve injuries, infection, swelling, no recurrence with no compromise in aesthetics and function in 5FU group
7	Layse Barreto Oliveira Borges et al[7]	39 patients Mean age -33 years	Angle and body of the mandible	Enucleation followed by adjuvant therapy	Decompression: 25 patients,7 enucleation with peripheral osteotomy,1 underwent enucleation with Carnoy's solution	———	three out of the 4 cases treated with enucleation and curettage had relapsed (75%). Recurrences were found in 3 lesions treated with enucleation and peripheral ostectomy (43%) as well as in 2 others treated with decompression and enucleation combined with	NIL

							peripheral ostectomy (9%). In those cases, in which decompression and further enucleation with Car noy's solution were performed, no recurrence was found	
8	Nicholas al[8] of,	32 patients ,	Anterior body and ramus of the mandible	Enucleation followed by adjuvant therapy-	Modified carnoys and 5 FU	NA	No recurrence in 5 FU group 4 recurrences in Modified carnoy's solution	NIL

Discussion

OKC being the most aggressive odontogenic cyst having more incidence of recurrence and requires an invasive management, proper diagnosis and management. Primary surgical management with the use of appropriate adjuvant therapy is the key for reducing the rates of recurrence. The most efficient way to treat OKC is marsupialization followed by enucleation for large lesions or only enucleation for smaller lesions followed by removal of all the remnants of daughter cells causing recurrence. Various adjuvant therapy is used post enucleation of the cyst including the Carnoy's solution, Modified Carnoy's, peripheral osteotomy, cryosurgery, phototherapy and 5FU.Among all this the use of Carnoys and its modification, and 5FU is widely used post enucleation with or without marsupialization. In this study we compare the efficacy of various adjuvant therapy used post enucleation in patients diagnosed with odontogenic keratocyst based on the study of various articles and scientific databases . 8 articles were included in the study based on the inclusion criteria. In all the articles included, the primary treatment followed for Odontogenic keratocyst involving mandible i.e.: over the anterior mandible, angle and ramus of the mandible was enucleation with or without marsupialization followed by use of adjuvant therapy such as carnoy's solution ,modified carnoys,5FU ,Cryo-surgery and peripheral osteotomy . The mean age of the patients were 35 years and the follow-up period was 2-6 years. There was a low recurrence rate in cases where 5FU has been used as an adjuvant therapy compared to patients who underwent adjuvant therapy involving peripheral osteotomy and modified carnoy's solutions. Modified carnoy's solution shows incidence of permanent nerve paraesthesia and swelling post operatively. Peripheral osteotomy alone after enucleation shows recurrence but when combined with carnoy's solution shows less recurrence. 5FU showed lower recurrence rate and associated complications as it's an antimetabolite that targets the proliferative cells. The pharmacologic effect of 5-FU is affected by 3 enzymes: TS, TP, and dihydropyridine dehydrogenase and 5-FU is not known to be neurotoxic thus in our study we conclude that 5FU has high efficacy as adjuvant therapy when compared with Carnoys, modified carnoys and peripheral osteotomy.

Conclusion:

Odontogenic Keratocyst being aggressive in nature requires proper diagnosis and treatment planning. The primary treatment plan being enucleation with or without marsupialization followed by various adjuvant therapy such as use of carnoy's solution, modified carnoy's solution, 5FU,Peripheral osteotomy cryotherapy and phototherapy. Most commonly used adjuvant therapy are carnoy's solution, modified carnoy's solution and 5FU. In this study we conclude that 5FU is a targeted therapy for odontogenic keratocyst when compared to other adjuvant therapies because of its minimal recurrence rate, bio-compatibility thereby reducing post-surgical morbidity. Further prospective studies using 5FU, longer follow-up times , and comparison of the use of 5FU with other effective and emerging therapies for OKCs.

Compliance with ethical standards

Conflict of interest: Nil

Ethical approval: Not applicable

Informed consent: Not applicable

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