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Research Article

Conservative Treatments of Keratocystic Odontogenic Tumors

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Abstract

Various treatment modalities have been reported for keratocystic odontogenic tumors (KOTs), with different recurrence rates. Enucleation is the complete removal of the cystic lining, but due to the thin and friable lining, the complete removal of KOT become difficult [1].The high recurrence rate after simple enucleation is caused by the presence of retained fragments of lining plus daughter cysts that are left behind [2]. There are adjunctive conservative treatments used with enucleation to decrease the recurrence rate of KOTs. Enucleation with curettage is Additional removal of bone tissue at the periphery by 1 - 2 mm after cyst excision by using curette or rotary instrument [1]. Enucleation with Carnoy's solution After enucleation of KOT,the bone cavity is treated with Carnoy's solution, The solution penetrates in the cancellous space of the bone in 3 - 5 min by approximately 1.54 mm, fixating and eliminating the remaining tumor cells [3]. Enucleation with liquid nitrogen cryotherapy After removal of the tumor lining, the bone cavity is treated with liquid nitrogen at temperature up to (–196.6°C) [4]. Unfortunately, cryotherapy leads to the formation of intracellular and extracellular ice crystals that disrupt normal intracellular osmotic and electrolyte balance, which ultimately causes cell death [5].

Objective: This study aimed at comparing the recurrence rate between enucleation with curettage, enucleation with carnoy's solution and enucleation with liquid nitrogen cryotherapy. Also to show our suggestion that ultrasonic technique can be use as an efficient tool for curettage KOTs.

Materials and Methods: This is a systematic review study. The research sources utilized were PubMed, Google scholar, MEDLINE and Complutense university Library. The keywords which were selected based on Medical Subject Heading (MeSH) terms and PICOS criteria were odontogenic keratocyst, Keratocystic odontogenic tumor AND enucleation OR curettage or Carnoy's solution or liquid nitrogen cryotherapy And ultrasonic or ultrasound or piezoelectric. For the period from 2001 to 2019. Statistical analyses were performed to compare the recurrence rate between enucleation with curettage, enucleation with carnoy's solution and enucleation with liquid nitrogen cryotherapy

Results: The total number of subjects that underwent Enucleation with curettage, carnoy's solution and liquid nitrogen cryotherapy was 954. In 431 subjects who had enucleation with curettage, 88 subjects had recurrence (19.9%). In 456 subjects who had enucleation with carnoy's solution 36 had recurrence (7,8%). In 67 subjects who had enucleation with liquid nitrogen cryotherapy 5 had recurrence (7,4%).

Conclusion: This systematic review appears that There was no a significant difference in the recurrence rate between enucleation with carnoy's solution group and liquid nitrogen cryotherapy group. However, the higher recurrence rate was for enucleation with curettage. group. In addition, study appears the advantages of ultrasonic technique in surgical field and suggest that ultrasonic technique can be a conservative tool of curettage to minimize the recurrence rate of Keratocystic Odontogenic Tumors.

Keywords: Conservative; Keratocystic; Odontogenic; Tumors

Introduction

Keratocystic odontogenic tumor (KOT) is locally aggressive with a high recurrence rate compared to other odontogenic cysts and neoplasms. KOTs have the tendency to invade adjacent tissues [6].

It was described by Philipsen in 1956 as an odontogenic keratocyst [7]. Keratocystic Odontogenic Tumor was named in 2005, when the World Health Organization termed Keratocystic Odontogenic Tumor over odontogenic keratocyst which had been used as a traditional term [8] based on evidence of various clinicopathological studies [9].

Keratocystic odontogenic tumors (KOTs), are benign, intraosseous, cystic lesions of odontogenic origin with high growth potential and propensity for recurrence [9], most of KCOTs occur in isolation as single, non-syndromic cysts, they may also present as multiple cysts as a feature of the nevoid basal cell carcinoma syndrome (NBCCS). NBCCS, also known as Gorlin syndrome [9].

KOTs arise from remnants of dental lamina, an embryonic structure that normally differentiates into tooth buds and enamel producing cells during odontogenesis. The remnants of dental lamina usually regress at later stages of development [10].

The tumour has a predilection for the mandibular 3rd molar region and usually manifest as multilocular radiolucencies with scalloped well defined margins [11]. Aspiration biopsies reveal keratin flakes with protein levels \4 g/100 ml. Radiography Classically the KOT has been shown to have a definite radiolucent entity with well defined borders extending along the cancellous bone. It can either be a unilocular or multilocular entity [11].

Management options in KOT can broadly be divided into conservative treatment and radical management [9]. Treatments modalities have been reported with differing recurrence rates. Enucleation [12], enucleation with cryotherapy [13], enucleation with carnoy's solution [1], marsupialization [14], decompression [15] and resection [16].

Curettage After enucleation KOT. Curettage is removal of bone tissue at the periphery by 1 - 2 mm after cyst excision by using curette or rotary instrument, it is difficult to estimate how much bone to remove with rotary instrument. The main advantage of the curette that is controllable by the surgeon. Some surgeons use methylene blue or crystal vilet (or any other vital stain) for visualization of the neoplasm retained lining for complete resection during curettage [2].

Carnoy's solution After enucleation KOT. Carnoy's solution was first used as a medicament in surgery by Cutler and Zollinger in 1933 [17]. Originally used as a histologic fixative2. The solution penetrates into cancellous space of the bone in 3 - 5 min by approximately 1.54 mm, fixaing and eliminating the remaining tumor cells [3]. Treatment of the bone cavity with Carnoy's solution and its modifications should not exceed 2 - 3 min because of the nonselective effect of this substance on the surrounding soft tissues and neurovascular bundles, Then should be actively washed out of the bone cavity with saline [1].

Cryotherapy After enucleation KOT and removal of the tumor lining, the bone cavity is treated with liquid nitrogen the temperature is(–196.6°C) [15]. Unfortunately, cryotherapy leads to the formation of intracellular and extracellular ice crystals that disrupt normal intracellular osmotic and electrolyte balance, which ultimately causes cell death [5]. After careful enucleation, liquid nitrogen is applied to the walls of the formed cavity for at least 1 min until the cavity covered with a layer of ice. Studies have shown that the penetration depth of liquid nitrogen into bone tissue is at least 1.5 mm [2]. This substance is very aggressive to soft tissue, vascular, nerve bundles, dental tissue1 and does significantly weaken in bone until new osteogenesis occurs [2].

Keratocystic odontogenic tumors (KOT) have a high rate of recurrence and very limited treatment options beyond surgery[11]. We always need to more conservative and efficient techniques and approaches to minimized the recurrence rate of KOTs. We suggest that Ultrasonic can be used as an efficient tool to minimized the recurrence rate of KOTs.

The concept of ultrasonic bone dissection was envisioned in 1960s by McFall, In 2001. Vercellotti introduced an angled piezoelectric short saw, which presented benefits for osteotomies during oral surgery without causing damage to adjacent soft tissue. Ultrasonic systems have been used for surgical soft tissue removal for several decades [18]. These devices have gained widespread acceptance in dentistry, neuro,orthopedic, ophthalmic, plastic, and maxillofacial surgeries [19].

Materials and Methods

Description of search strategy of relevant literature Objective The objective of this study was to compare the recurrence rate between three treatments modalities of Keratocystic Odontogenic Tumors (KOTs), enucleation with curettage, enucleation with carnoy's solution and enucleation with liquid nitrogen cryotherapy. And to show our suggestion that ultrasonic device can be used as an effective adjunctive conservative tool for curettage after enucleation in KOTs treatments.

Criteria for considering studies (PICO)

The studies considered for inclusion in this literature review include case series, cohort studies, and randomized clinical trial studies (Table 1).

Parameters for eligible studies
P Patients who had non-syndromic KOT
I Enucleation with curettage, enucleation with carnoy's solution and enucleation with liquid nitrogen cryotherapy
C Curettage after enucleation Carnoy's solution after enucleation Liquid nitrogen cryotherapy after Enucleation
O Recurrence rate
P, population; I, intervention; C, control; O, outcome

Table 1: Issues of interest based on study population, intervention, control group and outcome measures (PICO).

Search strategies

The PubMed (MEDLINE) database, Universidad de Complutense Library,Google scholar and Scopus. The keywords were selected based on Medical Subject Heading (MeSH) terms and PICOS criteria. The keywords for search included: odontogenic keratocyst, Keratocystic odontogenic tumors and enucleation and curettage Or enucleation and carnoy's solution Or enucleation and liquid nitrogen cryotherapy Or marsupialization OR decompression OR cystectomy. To avoid missing an article, the references of each selected manuscript was rechecked manually through Mendeley Program.

Inclusion criteria

A protocol was used for establishment of the inclusion and exclusion criteria. Full-text articles in English language were assessed for the following inclusion criteria including

1. Patients who had non-syndromic KOTs.
2. The technique was enucleation with curettage or enucleation with carnoy's solution or enucleation with liquid nitrogen cryotherapy
3. The follow-up time was documented. Studies were excluded if they were animal or in vitro studies. Duplicate publications (risk of bias), syndromic KOTs or articles without histopathological diagnosis information of each patient were removed from the study.

Statistical analysis

The statistical analyses were conducted using the IBM statistical SPSS 64- bit edition for Microsoft, version 26 (IBM, USA).

Evaluation of papers and level of evidence

In an initial research, 2322 articles were identified through electronic database. After removing duplications 1122 articles were evaluated. The total subject(KOTs) number was 954 in 26 articles (Table 2). The medium follow up time was between 6 months to more than 5 years. The number of subjects who treated by enucleation with curettage was 431,456 subjects treated by enucleation with carnoy's solution and 67 subjects treated by Liquid nitrogen cryotherapy after enucleation.

In 431 subjects who had enucleation with curettage, 86 subjects had recurrence (19.9%). In 456 subjects who had enucleation with carnoy's solution 36 had recurrence (7,8%). In 67 subjects who had enucleation with liquid nitrogen cryotherapy 5 had recurrence (7,4%).

In addition, in this study we took information from different articles, case series and casa reports sources about ultrasonic technique in different surgical fields as spinal, neuro and maxillofacial surgeries. with different ultrasonic devices and tips as ultrasonic bone curette, sonopet ultrasonic curette, bone scalpel ultrasonic and piezosurgery. To evaluate if the ultrasonic technique cause damage in soft tissue (vessels, nerves and mucosa), bleeding and to evaluate the cutting efficacy. There are many articles that talking about the ultrasonic technique in surgical field. But this is the first study talking about using the ultrasonic curette as a tool of curettage Keratocystic Odontogenic Tumor.

Author	Year	Cyst N	Treatment	Follow Up	Recurrence N/R
Alstad [20]	2017	9	Enuc+Curettage	82	3(33.3%)
Boffano [21]	2010	250	Enuc+Curettage	36	28(11.2%)
Cakur [22]	2008	1	Enuc+Curettage	6	0(0%)
Hupp [6]	2006	11	Enuc+Carnoy,s	>5 Year	1(9%)
Dashow [23]	2013	80	Enuc+Curettage	>5 Year	36(45%)
Driemel [24]	2007	17	Enuc+Curettage	114	3(17.6%)
Gosau [25]	2010	14	Enuc+Carnoy,s	102	2(14.2%)
Güler [26]	2012	10	Enuc+Carnoy,s	41	0(0%)
Kolokythas [7]	2007	11	Enuc+Curettage	>5 Year	0(0%)
Leung [27]	2016	105	Enuc+Carnoy,s	87	12(11.4%)
Macdonald [28]	2013	3	Enuc+Cryotherapy	108	2(66.6%)
Madras [29]	2008	22	Enuc+Curettage	>5 Year	6(27.2%)
Maurett [30]	2006	10	Enuc+Curettage	25	2(20%)
Morgan [31]	2005	11	Enuc+Curettage	>5 Year	6(54.5%)
	2005	2	Enuc+Carnoy,s	>5 Year	1(50%)
O Ribeir [32]	2012	56	Enuc+Carnoy,s	42	0(0%)
Rao [33]	2014	30	Enuc+Carnoy,s	56	2(6.6%)
Ribeiro [34]	2012	22	Enuc+Carnoy,s	43	1(4.5%)
Sanchez [35]	2014	2	Enuc+Carnoy,s	108	2(100%)
Schmidt [13]	2001	49	Enuc+Cryotherapy	42	3(6.1%)
Selvi [36]	2012	20	Enuc+Curettage	38	2(10%)
Stoelinga [37]	2001	43	Enuc+Carnoy,s	>5 Year	3(6.9%)
Titinch [38]	2012	8	Enuc+Carnoy,s	20	3(37.5%)
Zhao [39]	2012	124	Enuc+Carnoy,s	60	7(5.6%)
Zhou [40]	2014	1	Enuc+Cryotherapy	8	0(0%)
Zhou [41]	2005	10	Enuc+Cryotherapy	>5 Year	0(0%)
Peterson [42]	2002	29	Enuc+Carnoy,s	>5 Year	2(6.8%)

Table 2

Discussion

Keratocystic Odontogenic Tumor has aggressive clinical behavior, local tissue distraction and the high recurrence rate [11]. Defined as unicystic or multicystic intraosseous neoplasm [43], of odontogenic organ lining (parakeratinized stratified squamous epithelium) and has infiltrative behavior [9].

The characteristic features of KOTs are high recurrence rate,high growth rate, ability to resorb bone and secondary teeth displacement [44]. Consider 11% of maxillofacial cysts, most commonly in the mandibular ramus and the angel of mandible, grow along the cancellous channel of cancellous bone with a little cortical expansion (expand mesio distaly) by releasing the inflammatory cytokines like IL-1 to of the epithelium to activate the bone resorption around the tumor by stimulating the Osteoclastogenesis. There are theories described the etiology of KOT, the most probably is a development of the remnant of dental lamina.

The treatment modalities of KOTs have evoked the greatest debates and controversies because of the recurrence potential of the tumor. Management of KOT should focus on selecting the

best modality that carries the lowest possible risk of recurrence and minimum morbidity [11]. Management of KOT remains controversial owing to multiple different treatment protocols with varying recurrence rates [3].

Resection generally has been reserved for patients who have undergone several surgical procedures to remove the same recurring KOT and patients who tend to require long follow-up because of the nature of KCOT and its intrinsic position in nevoid basal cell carcinoma syndrome (NBCCS) [3]. Resection associated with the lowest recurrence rate of KOTs. However, this treatment option leads to high percentage of patient disability1 and may cause excessive morbidity [2].

Marsupialization was originally described by Partsch in the late 1800s as a definitive treatment for cysts at a time when antibiotics were not available and enucleation and primary closure most often led to wound breakdown and infection [14]. Usually this technique used for large lesions. by opening up the cyst to the oral cavity and suturing the cyst lining to the oral mucosa [45].

Enucleation alone is not sufficient. Adjunctive treatment has been proposed in addition to the surgical enucleation, such as curettage, cryotherapy (liquid nitrogen) and the fixative Carnoy's solution,which attempt to remove residual tissue to prevent KOTs recurrence [46].

Carnoy's solution is potent fixative, hemostatic, and cauterization agent that penetrates cancellous spaces in the bone (the average penetration depth is approximately 1.54 mm in 5 min after application on the bone tissue) and ensures removing the remaining cells of the cystic lining [47] consist of Ferric chloride Chloroform, Glacial acetic acid and Ethyl alcohol. Most surgeons do not use chloroform in the composition of Carnoy's solution since chloroform triggers malignant transformation of cells and causes infertility1. In this study enucleation with carnoy's solution showed recurrence rate (7,6%) (Table 2). However, carnoy's solution is nonselective fixative and the effect involves both tumor cells and the surrounding tissues including blood vessels and nerves [1]. Cryotherapy cause KOTs cells death by freezing at temperatures less than –20C. The only commonly available agent that can achieve this temperature is liquid nitrogen, which boils at –196C. Carbon dioxide and nitrous oxide both boil at temperatures high enough (–78.5C and –89.7C) that they cannot maintain-20C consistently [2]. Studies have shown that liquid nitrogen penetrates to at least 1.5 mm around the cavity [48]. In this study enucleation with cryotherapy showed recurrence rate (7,4%) (Table 2). However, regarding to (Schmidt BL) they used enucleation with cryotherapy and inferior alveolar nerves were involved by Liquid nitrogen, most patients achieved at least return part of sensation and many patients achieved full return of sensation [49]. When teeth are affected by cryotherapy, degenerative changes can occur in pulpal tissues [2]. Liquid nitrogen cryotherapy does significantly weakening in the bone until new osteogenesis occurs [2].

Curettage is removal of bone tissue at the periphery by 1 - 2 mm after cyst excision by using curette or rotary instrument, is difficult to estimate how much of bone were removed with the conventional drill for this some surgeons use methylene blue or crystal violet (or any other vital stain) for visualization of the neoplasm retained lining for complete resection2. In this study enucleation with curettage showed highest recurrence rate (20,3%) (Table 2). According to (Al-Moraissi, Ahmed large systematic review and meta-analysis) [43] they evaluated the recurrence rate of the current treatment plans of KOTs and the results were enucleation alone (23.1%), enucleation with curettage (17.4%), enucleation and Carnoy's solution (11.5%), enucleation plus liquid nitrogen cryotherapy (14.5%), marsupialization alone (32.3%), decompression followed by residual cystectomy (14.6%), and resection (8.4%) [43].

As we showed in this study, KOTs have more then plan of treatment because the recurrence potential of the tumor. Every plane of treatment has advantages and disadvantages. Enucleation with curettage showed high recurrence rate, could be for, the less of effectiveness of manual curette or the difficulty in controlling and estimating how much of bone were removed with the conventional drill. In this study we suggest that ultrasonic technique (Ultrasonic bone curette, Sonopet ultrasonic,bone scalpel ultrasonic or Piezosurgery ultrasonic) can be an effective tool of KOTS treatment.

Ultrasonic

The first used of the ultrasonic equipment in dental field was for dental plaque removal [50]. Then have been developed in many medical uses like ear surgery, nose surgery, throat surgery, spine surgery, neurosurgery and oral and maxillofacial surgery [19].

The ultrasonic machine produce longitudinal vibration can be from 120 to 365mm at an ultrasonic frequency of 25 KHz

and connected with coolant system near to the working tip [51]. Ultrasonic micro vibrations created by the piezoelectric effect (certain ceramics and crystals deform when an electric current is passed across them, resulting in oscillations of ultrasonic frequency) [52]. Piezoelectric was described by Jean and Marie Curie in 1880 [52].

Ultrasonic systems have been used for surgical soft tissue removal for several decades. Typical applications include laparoscopic dissection, resection of head and neck tumours, lipoplasty and aspiration of spinal and intracranial tumours [18]. Numerous comparative studies have been performed to determine the safety and efficiency of ultrasonic technique in bone surgery [18].

Ultrasonic machine decreased the risk of damage of surrounding soft tissue and the critical structure like nerves, vessels and mucosa during surgeries [53]. This equipment is lightweight, safe, and easy in surgical operation. Ultrasonic technique performed clear operative field for surgeons by perform bone resection using both hands [50].

In the field of neurosurgery, ultrasonic instruments used for removing brain tumors such as gliomas, meningiomas, and neuromas [50] ultrasonic bone curette safe and simple during Anterior clinoidectomy and opening of the internal auditory canal, no performed damage to surrounding brain tissue, cranial nerves, or blood vessels as result of heat or vibration. Operations in deep areas can be performed without feeling psychomotor stress. This equipment should contribute to the development of a new modality for cranial base surgery.

During cranial base surgery, high- speed drills cause heat injury to cranial nerves, blood vessels, and normal brain tissue and support from assistants usually is required [50]. Drilling can cause temperature elevation of the bone to 70°C around the tip of the drill, so continuous irrigation with cool-controlled fluid is required to prevent thermal damage to surrounding normal tissue. When resecting hard bone with a high-speed drill, the surgeon sometimes must hold the drill with both hands to prevent damage to surrounding tissue caused by unexpected motion of the drill. Surgery is frequently interrupted by irrigation, suction, and coagulation procedures [50]. In the other hand, ultrasonic instruments used in brain tumors removal such as gliomas, meningiomas, and neuromas [50]. Ultrasonic bone curette obviates the need of assistants support by allowing the surgeon use both hands during osteotomy, need minimal pressure in resection, through simple scratching motions toward the surgeon, as with a curette [50]. Ultrasonic machine preformed fast bone Resection and evacuation of bone dust with cool-controlled irrigation fluid to make the operative field clear [50] heat production associated with the use of the ultrasonic bone curette in surrounding bone would not be high because cool-controlled irrigation fluid (20°C) was used during surgery. ultrasonic bone curette more useful and safe in cranial base surgery than high-speed air drill [50].

Using of ultrasonic bone curette for optic canal unroofing and anterior clinoidectomy, the device specifically affect the hard tissue such as bone and left the soft tissue such as the dura mater, ultrasonic bone curette made the procedure easy and safe [54].

Sonopet ultrasonic bone curette minimize ocular complications as soft tissue damage, infection, inflammation, and visual loss in orbital decompressions and dacryocystorhinostomies surgeries, and removed the bone effortlessly with precise control and maintain Visualization [55].

In the field of Maxillofacial, ultrasonic bone curette can be used in pterygoid plates osteotomy in cases of Le Fort 1 osteotomy safely with minimal bleeding and complications [51]. Ultrasonic bone curette (Sonopet) is safe method for making a guiding groove with minimal bleeding, complications and without causing damage to surrounding tissue [56]. Bone scalpel ultrasonic osteotomy minimized the occurrence of nerve impairment and bad splits and in the other side improve the control in orthognathic surgery osteotome [18].

Ultrasonic bone curette described as device allowed surgeons to remove bone without causing damage to the surrounding tissue as inferior alveolar nerve [19]. ultrasonic bone curette offering potential for greater bone cutting precision and less damage to surrounding soft tissue more than the conventional high speed drill in spinal surgeries [57]. using piezosurgery ultrasonic device in cases of radicular cysts as tool of enucleation minimize complications [58].

As we showed in this study Keratocystic Odontogenic Tumors have high recurrence probability, specially with enucleation and

curettage.We suggest that ultrasonic device can decrease the recurrence rate in a way more conservative than the others plans of treatments. This is the first article talk about the ultrasonic as tool of treatment for Keratocystic Odontogenic Tumors.some studies have to evaluate the technique and the recurrence rate clinically, and this is will be the objective of our next study

Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

Conclusion

This systematic review appears that There was no a significant difference in the recurrence rate between enucleation with carnoy's solution group and liquid nitrogen cryotherapy group. However, the higher recurrence rate was for enucleation with curettage. group. In addition, study appears the advantages of ultrasonic technique in surgical field and suggest that ultrasonic technique can be a conservative tool of curettage to minimize the recurrence rate of Keratocystic Odontogenic Tumors.

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Bibliography

1. Lebedev VV and Butsan SB. "The Use of Carnoy ' s Solution and Its Modifications for Reducing the Number of Recurrences after Surgical Removal of Keratocystic Odontogenic Tumors and Ameloblastomas : A Systematic Review". *Moscow University Biological Sciences Bulletin* 74.2 (2019):108-116.

2. Pogrel MA. "The Keratocystic Odontogenic Tu m o r". *Oral and Maxillofacial Surgery Clinics of North America* 25.1 (2013): 21-30.

3. Johnson NR., *et al*. "Management and recurrence of keratocystic odontogenic tumor: A systematic review". *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* 116.4 (2013): e271-e276.

4. Salmassy DA and Pogrel MA. "Liquid nitrogen cryosurgery and immediate bone grafting in the management of aggressive primary jaw lesions". *Journal of Oral and Maxillofacial Surgery* 53.7 (1995): 784-790.

5. Tonietto L., *et al*. "Enucleation and liquid nitrogen cryotherapy in the treatment of keratocystic odontogenic tumors: A case series". *Journal of Oral and Maxillofacial Surgery* 69.6 (2011): e112-e117.

6. Hupp JR., *et al*. "Review of odontogenic keratocysts and the behavior of recurrences". *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* 101 (2006): 5-9.

7. Kolokythas A., *et al*. "Odontogenic Keratocyst: To Decompress or Not to Decompress? A Comparative Study of Decompression and Enucleation Versus Resection/Peripheral Ostectomy". *Journal of Oral and Maxillofacial Surgery* 65.4 (2007): 640-644.

8. Antonoglou GN., *et al*. "Non-syndromic and syndromic keratocystic odontogenic tumors: Systematic review and meta-analysis of recurrences". *Journal of Cranio-Maxillofacial Surgery* 42.7 (2014): e364-e371.

9. Menon S. "Keratocystic Odontogenic Tumours: Etiology, Pathogenesis and Treatment Revisited". *Journal of Oral and Maxillofacial Surgery* 14.3 (2015): 541-547.

10. Qu J., *et al*. "Underestimated PTCH1 mutation rate in sporadic keratocystic odontogenic tumors q". *Oral Oncology* 51 (2015): 40-45.

11. Amm HM Devilliers P., *et al*. "Targeting the Sonic Hedgehog Pathway in Keratocystic Odontogenic Tumor * Changchun Ren". *Journal of Biological Chemistry* 287.32 (2012): 27117-27125.

12. Singh M and Gupta KC. "Surgical treatment of odontogenic keratocyst by enucleation". *Contemporary Clinical Dentistry* 1.1 (2010): 263-268.

13. Schmidt BL and Pogrel MA. "The Use of Enucleation and Liquid Nitrogen Cryotherapy in the Management of Odontogenic Keratocysts". *Journal of Oral and Maxillofacial Surgery* 59 (2001): 720-725.

14. Pogrel MA and Jordan RCK. "Marsupialization as a Definitive Treatment for the Odontogenic". *Journal of Oral and Maxillofacial Surgery* 62.6 (2004): 651-655.

15. Peterson ELJ. "Treatment of large odontogenic keratocysts by decompression and later cystectomy". *Oral Surgery, Oral Medicine Oral Pathology Oral Radiology and Endodontology* 82.2 (1996): 122-131.

16. Williams TP and Jr FAC. "Surgical Management of the Odontogenic Keratocyst: Aggressive Approach". *Journal of Oral and Maxillofacial Surgery* 52.9 (1994): 964-966.

17. Cutler EC and Zollinger R. "The use of sclerosing solutions in the treatment of cysts and fistulae". *The American Journal of Surgery* (1933): 3.

18. Gilles R., *et al*. "Ultrasonic orthognathic surgery: enhancements to established osteotomies". *International Journal of Oral and Maxillofacial Surgery* 12.4 (2012).

19. Garzino-Demo P., *et al*. "The Use of an Ultrasonic Bone Curette in the Surgery of Jaw Tumors Involving the Inferior Alveolar Nerve". *International Journal of Oral and Maxillofacial Surgery* 69 (2011): e100-e104.

20. Alstad V and Abtahi J. "Surgical removal of keratocystic odontogenic tumours via a Le Fort I osteotomy approach: a retrospective study of the recurrence rate". *International Journal of Oral and Maxillofacial Surgery* 46.4 (2017): 434-439.

21. Boffano P., *et al*. "Keratocystic Odontogenic Tumor (Odontogenic Keratocyst): Preliminary Retrospective Review of Epidemiologic, Clinical, and Radiologic Features of 261 Lesions From University of Turin". *Journal of Oral and Maxillofacial Surgery* 68 (2010): 2994-2999.

22. Çakur B, Milog Ö., *et al*. "Keratocystic odontogenic tumor invading the right maxillary sinus: a case report". *Journal of Oral Science* 50.3 (2008): 345-349.

23. Dashow J., *et al*. "Keratocystic Odontogenic Tumor Recurrence Rates With Enucleation and Curettage Using Carnoy' s Versus Modified Carnoy' s Solution Submandibular Gland Transfer in the Treatment of Severe Dry Eye Syndrome The Use of Custom 3D Anatomical Spacers in Maxillo". *International Journal of Oral and Maxillofacial Surgery* 71.9 (2013): e4-e5.

24. Driemel O., *et al*. "Originalien Vergleichende klinische und immunhistochemische Charakterisierung keratozystischer odontogener Tumoren und Ameloblastome im Hinblick auf das Rezidivrisiko". *Mund Kiefer Gesichts Chir* 12.4 (2007).

25. Gosau M., *et al*. "Two modifications in the treatment of keratocystic odontogenic tumors (KCOT) and the use of Carnoy's solution (CS)-a retrospective study lasting between 2 and 10 years". *Springer* 14.1 (2010): 27-34.

26. Güler N and Demirkol A. "The cientificWorld Journal Clinical Study Conservative Management of Keratocystic Odontogenic Tumors of Jaws". *The Scientific World Journal* (2012):1-10.

27. Leung YY., *et al*. "Results of the treatment of keratocystic odontogenic tumours using enucleation and treatment of the residual bony defect with Carnoy's solution". *Journal of Oral and Maxillofacial Surgery* 45 (2016): 1154-1158.

28. MacDonald D., *et al*. "Can clinical and radiological features predict recurrence in solitary keratocystic odontogenic tumors?" *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* 115 (2013): 263-271.

29. Madras J and Lapointe H. "Keratocystic Odontogenic Tumour: Reclassification of the Odontogenic Keratocyst from Cyst to Tumour" 74 (2008).

30. Maurette PE., *et al*. "Conservative Treatment Protocol of Odontogenic Keratocyst: A Preliminary Study". *Journal of Oral and Maxillofacial Surgery* 64 (2006): 379-383.

31. Morgan TA., *et al*. "A Retrospective Review of Treatment of the Odontogenic Keratocyst". *Journal of Oral and Maxillofacial Surgery* 63 (2005): 635-639.

32. Ribeiro Junior O., *et al*. "Keratocystic odontogenic tumors and Carnoy's solution: results and complications assessment". *Journal of Oral Diseases* 18.6 (2012): 548-557.

33. Rao K and Kumar S. "The Use of Enucleation and Chemical Cauterization (Carnoy's) in the Management of Odontogenic Keratocyst of the Jaws". *Indian Journal of Otolaryngology and Head and Neck Surgery* 66.1 (2014): 8-12.

34. Ribeiro Junior O., *et al.* "Keratocystic odontogenic tumors and Carnoy's solution: results and complications assessment". *Journal of Oral Diseases* 18 (2012): 548-557.

35. Sánchez-Burgos R., *et al*. "Clinical, radiological and therapeutic features of keratocystic odontogenic tumours: A study over a decade". *Journal of Clinical and Experimental Dentistry* 6.9 (2014): 259-264.

36. Selvi F., *et al*. "Keratocystic Odontogenic Tumors: Predictive Factors of Recurrence by Ki-67 and AgNOR Labelling". *International Journal of Medical Sciences* 9.4 (2012):262-268.

37. Stoelinga. "Long-term follow-up on keratocysts treated according to a defined protocol". *International Journal of Oral and Maxillofacial Surgery* 30.1 (2001): 14-25.

38. Titinchi F and Nortje CJ. "Keratocystic odontogenic tumor: a recurrence analysis of clinical and radiographic parameters". *Oral and Maxillofacial Radiology* 114.1 (2012):136-142.

39. Zhao Y., *et al*. "Recurrent keratocystic odontogenic tumours: report of 19 cases". *Dentomaxillofacial Radiology* 41 (2012): 96-102.

40. Zhou J., *et al*. "Giant keratocystic odontogenic tumor of the maxillary sinus and zygoma : A case report". *Oncology Letters* 8 (2014): 2675-2677.

41. Zhou Jiao J., *et al*. "Treatment of Recurrent Odontogenic Keratocyst with Enucleation and Cryosurgery: A Retrospective Study of 10 Cases". 14 (2005).

42. Peterson LJ., *et al*. "Oral and Maxillofacial Surgery Treatment of odontogenic keratocysts: A follow-up of 255 Chinese patients". *Journal of Oral and Maxillofacial Surgery* 94.2 (2002).

43. Al-Moraissi A., *et al*. "What surgical treatment has the lowest recurrence rate following the management of keratocystic odontogenic tumor?: A large systematic review and meta-analysis". *Journal of Cranio-Maxillofacial Surgery* 45 (2017): 131-144.

44. Gonz L. "Outcome after 8 years of a modi fi ed conservative treatment experience in keratocystic odontogenic tumor in 5 patients" *Oral and Maxillofacial Surgery Cases* 3 (2017): 42-47.

45. Tabrizi R., *et al*. "Decompression or Marsupialization; Which Conservative Treatment is Associated with Low Recurrence Rate in Keratocystic Odontogenic Tumors ?" *A Systematic Review* (2019):145-151.

46. Fnj S. "Interventions for the treatment of keratocystic odontogenic tumours (KCOT, odontogenic keratocysts (OKC)) (Protocol)". *Cochrane Library: Cochrane Reviews* 4 (2010).

47. Pitak-arnnop P and Oprean N. "Management of odontogenic keratocysts of the jaws: A ten-year experience with 120 consecutive lesions". *Journal of Cranio-Maxillofacial Surgery* 38.5 (2010): 358-364.

48. Technologies E. "Effects of liquid nitrogen cryotherapy and bone grafting on artificial bone defects in minipigs: a preliminary study". *International Journal of Oral and Maxillofacial Surgery* 31.3 (2002):296-302.

49. Schmidt BL and Pogrel MA. "Neurosensory Changes After Liquid Nitrogen Cryotherapy". *Journal of Oral and Maxillofacial Surgery* 62.10 (2004):1183-1187.

50. Hadeishi H., *et al*. "Anterior Clinoidectomy And Opening of The Internal Auditory Canal Using an Ultrasonic Bone Curette". *Neurosurgery* 52 (2003): 867-871.

51. Ueki K., *et al*. "Le Fort I osteotomy using an ultrasonic bone curette to fracture the pterygoid plates". *European Association for Cranio-Maxillofacial Surgery* 32 (2004): 381-386.

52. Eggers G., *et al*. "Piezosurgery ®: an ultrasound device for cutting bone and its use and limitations in maxillofacial surgery". *British Journal of Oral and Maxillofacial Surgery* 42.4 (2004): 51-453.

53. Labanca M., *et al*. "Piezoelectric surgery: Twenty years of use". *British Journal of Oral and Maxillofacial Surgery* 46 (2008): 265-269.

54. Han Soo Chang Md., *et al*. "Ultrasonic bone curettage for optic canal unroofing and anterior clinoidectomy". *Journal of Neurosurgery* 104 (2006): 621-624.

55. Sivak-Callcott JA., *et al*. "Ultrasonic Bone Removal with the Sonopet Omni A New Instrument for Orbital and Lacrimal Surgery". *Arch Ophthalmology* 123 (2005): 1595-1597.

56. Ueki K., *et al*. "Use of the Sonopet ultrasonic curettage device in intraoral vertical ramus osteotomy". 36 (2007): 745-747.

57. MohaMad Bydon., *et al*. "Safety of spinal decompression using an ultrasonic bone curette compared with a high-speed drill: outcomes in 337 patients". *Journal of Neurosurgery Spine* 18 (2013): 627-633.

58. Kocyigit ID., *et al*. "Piezosurgery Versus Conventional Surgery in Radicular Cyst Enucleation". *Journal of Craniofacial Surgery* 23.6 (2012):1805-1808.