Clin Oral Invest (2010) 14:719–721
DOI 10.1007/s00784-010-0465-z

LETTER TO THE EDITOR

Enucleation of keratocystic odontogenic tumours: study interpretation, technical refinement and future research

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Received: 7 January 2010 / Accepted: 27 August 2010 / Published online: 14 September 2010

To Editor:
I read with interest the excellent article by Gosau et al. [1] on the treatment of keratocystic odontogenic tumours (KCOT) and would like to comment on that article regarding the study interpretation, technical refinement and future research.

1. Those authors reported a retrospective cohort study on 36 KCOT in 34 patients, 14 lesions of which were treated with enucleation and Carnoy's solution. The findings based on a small sample size may fail to detect statistical significance, so-called ‘type II error’. Significance may be achieved only if chance exaggerates any true differences between the groups under study and thus the study becomes ‘lack of power’. To detect a 50% to 80% relative efficacy benefit of one treatment over another, sample size in controlled therapeutic trials should range from 50 to 200 [2–5].
2. Voorsmit [6] originally recommended applying Carnoy's solution before enucleation. However, this might damage the specimen, as well as hampering the histopathological examination especially when there is ameloblastomatous or malignant transformation or secondary infection. Until now, there has not been strong evidence to support the use of Carnoy's solution before an enucleation of the cyst. Application of the Carnoy's solution after enucleation is more popular and unlikely to increase risks of tissue damage [7–9].
3. Carnoy's solution has caustic effect on adjacent tissues including nerves, and possible systemic toxicity. Moreover, chloroform has no longer been used because of its carcinogenicity [8, 9]. Preparation and the use of this solution therefore require particular attention. The failure to identify the inferior dental nerve injury may be due to the small sample size (14 lesions).
4. One speculation is that a high sample size lowers the recurrence rate after enucleation of OKCT, as seen in Table 1 of the article by Gosau et al. [1]. It is probable that surgeon experience on the enucleation correlates with the recurrence rate. Gosau et al. [1] revealed that 50% of KCOT (11 of 22) recurred unless Carnoy's solution was used, and large cysts tended to recur. Nonetheless, my previous publication based on 120 odontogenic keratocysts (OKC), 80 of which were KCOT, demonstrated that the recurrence rate of OKC after enucleation ‘without’ the use of Carnoy's solution was 26%. The size of 74 lesions exceeded 6 cm. Radiographic features, histological types (orthokeratocyst versus KCOT), lesion sizes, cortical perforation and sites of involvement were not individually significantly associated with the recurrence rate [9].

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5. In the Pitié-Salpêtrière University Hospital, multiple adjuncts have been used to minimise the recurrence rate of OKC, including aggressive curettage and/or peripheral ostectomy in cases of periapical presentation, surgical access difficulty or a recurrent cyst; removal of teeth within the cyst; close surveillance with the aid of computed tomography; and excision of overlying mucosa when cortices are perforated [8, 9]. More details on current status of the literature and our protocol for managing OKC and cyst-like lesions (expansile radiolucent lesions with no calcified matrix) of the jaws please refer to Pitak-Arnnop et al. [9].
6. Gosau et al. [1] revealed that the follow-up period ranged from 12 to 120 months, whilst they agreed that recurrences were common in the first 5 years after the initial enucleation. The follow-up periods between two groups (with versus without Carnoy's solution) were statistically significant: the patients treated with Carnoy's solution were followed up in the shorter period. Taken together, the benefit of Carnoy's solution remains unclear. A follow-up period less than 5 years is unlikely to be long enough to ensure a cure. In my previous publications, 695 odontogenic cysts were treated in the 10-year study period, ten of which were Gorlin's syndrome and 120 lesions were non-syndromic OKC. Thirty-two of the 37 OKCs recurred within 5 years, whereas three other OKCs recurred 15, 19 and 23 years after enucleation. Notably, other components of Gorlin's syndrome were identified in two of the ten patients after multiple recurrences of OKC many years later [9, 10]. This emphasises the importance of the long-term follow-up of the OKC patients.
7. Although oral and maxillofacial surgery has been progressing over the past decades, definite therapy on several conditions, such as OKC, ameloblastoma and osteoradionecrosis of the jaws, remains undecided. Most studies are level IV cohort studies: case series (no, or historical, control group). This may reflect the nature of surgery [5, 9, 11–13]. An obvious weakness of retrospective studies is a risk of bias that may overestimate or underestimate the study results. Observational studies do not control the exposure (intervention). Causal interference made in these types of studies is complicated by the contamination of unknown or unmeasured confounding variables [2–5]. The results between studies on KCOT treatments are somewhat difficult to compare because of the small sample sizes, retrospective nature, lack of treatment details and variable follow-up periods [7–9].
8. There is no question that patient's permission given under ‘unfair’ or ‘undue’ pressure is not consent: all potential risks, benefits and disadvantages of each treatment option must be informed and discussed. Surgeons must involve their KCOT patients in clinical decision-making [12, 14–17].
9. The Declaration of Helsinki suggests that a new intervention be tested against the ‘best current proven’ intervention [12, 14, 16, 17]. Unfortunately, there is a lack of consensus as to what constitutes universally accepted treatment for KCOT [7–9]. Therefore, further investigations must be designed and conducted carefully.

Considerations on these aspects in clinical practice and/or future research should be addressed when taking care of KCOT patients.

Disclosure of potential conflicts of interest The author indicates no potential conflicts of interest.

Financial disclosure There was no grant support for this letter.

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