Available online at www.sciencedirect.com
ScienceDirect
British Journal of Oral and Maxillofacial Surgery xxx (2017) xxx–xxx
BRITISH Journal of Oral and Maxillofacial Surgery
www.bjoms.com

Review

Volumetric comparison of autogenous bone and tissue-engineered bone replacement materials in alveolar cleft repair: a systematic review and meta-analysis

M. Kamal [a,b,*], A.H. Ziyab [c], A. Bartella [a], D. Mitchell [d], A. Al-Asfour [e], F. Hölzle [a], P. Kessler [b], B. Lethaus [a]

[a] *Department of Oral and Maxillofacial Surgery, RWTH Aachen University, Aachen, Germany*
[b] *Department of Cranio-Maxillofacial Surgery and GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands*
[c] *Department of Community Medicine and Behavioral Sciences, Kuwait University, Kuwait*
[d] *Maxillofacial Unit, Huddersfield Royal Infirmary, Huddersfield, United Kingdom*
[e] *Department of Surgical Sciences, Faculty of Dentistry, Kuwait University, Kuwait*

Accepted 2 May 2018

Abstract

The goal of reconstruction of the alveolar cleft in patients with cleft lip and palate is to improve the quality of tissue, the structural stability, and increase the volume of bone. This study is a systematic review with meta-analysis of volumetric bony filling using autogenous bone and various tissue-engineered bone substitutes. We made an electronic search on MEDLINE, EMBASE, SCOPUS, WEB OF SCIENCE, "grey" publications (materials and research produced by organisations outside traditional channels for commercial or academic publishing and distribution), and relevant cross references according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies that reported the outcomes of volumetric grafting were included in the meta-analysis. Of 1276 studies, 26 were included in the meta-analysis. Pooled analysis of 25 studies that used autogenous bone showed a significant reduction in the volume of the cleft equivalent to 62.0% bone fill (95% CI 54.3 to 69.6), in contrast to 10 studies that used a tissue-engineered material and reported bone filling of 68.7% (95% CI 54.5 to 82.8). The estimated sizes of pooled effects across studies showed that there was no significant difference between the two major intervention groups (p value 0.901). Our statistical analysis showed that autogenous bone grafts did not differ significantly from tissue-engineered materials in their ability to fill clefts.

Systematic review registration: International Prospective Register of Systematic Reviews, PROSPERO (CRD42017065045).

Keywords: cleft lip and palate; grafting; tissue-engineering; bone grafting; autogenous

Introduction

Cleft lip and palate is a malformation that is caused by the incomplete fusion of facial prominences during embryonic development. This results in a bony defect in the maxillary process and upsets the eruption of the teeth. Skeletal grafting of deformities in the alveolar cleft is an essential step in the re-

* Corresponding author at: Department of Oral and Maxillofacial Surgery, RWTH Aachen University, Pauwelsstraße 30, 52074 Aachen, Germany. Tel.: +49 241 8037172; Fax: +49 241 8099231.
E-mail address: mkamaldmd@ukaachen.de (M. Kamal).

https://doi.org/10.1016/j.bjoms.2018.05.007
0266-4356/

Please cite this article in press as: Kamal M, et al. Volumetric comparison of autogenous bone and tissue-engineered bone replacement materials in alveolar cleft repair: a systematic review and meta-analysis. *Br J Oral Maxillofac Surg* (2017), https://doi.org/10.1016/j.bjoms.2018.05.007

Table 1
Groups of grafting materials.

Autogenous bone grafts
1. Iliac crest
2. Mandibular
3. Cranial
4. Tibial
Tissue-engineered materials for bony replacement
1. Growth factors (bone morphogenetic protein, platelet-rich plasma, platelet-derived growth factor)
2. Improved scaffolds and cell treatment (mesenchymal stem cells, osteoblasts)/growth factors in combination
3. Biocomposites and haemostatic agents (fibrin glue, calcium phosphate, hydroxyapatite)

establishment of bony continuity of the alveolar arch, and the creation of favourable anatomy for dental rehabilitation.[1–3]

Reconstruction of these defects is done by grafting with autogenous bone, together with various tissue-engineered materials.[4–9] Autologous bone can be obtained from several donor sites including: iliac crest, calvarium, mandibular symphysis, mandibular ramus, and tibia, but each donor site carries its own unique risks and morbidity.[3,10]

A current review of published papers showed that many substitute materials are used to regenerate bone.[5–9,11] These can be categorised into groups (Table 1) based on their composition, which include:

Growth factors: biological factors based on molecular cellular interactions that improve osteogenesis. They include bone morphogenetic proteins, platelet-rich plasma, and platelet-derived growth factors.

Combination of improved scaffolds and cell treatment/growth factors: multiple scaffolds are used to promote osteoconduction. They are usually impregnated with cellular components, either mesenchymal stem cells or osteoblasts, which can also be treated with growth factor to increase bone formation further.

Biocomposites and haemostatic agents: biocompatible synthetic materials, or biological components that promote osteoconduction and improve the formation of blood coagulum, can improve delivery of growth factors and promote osteogenesis. Biocompatible alloplastic materials include calcium phosphate and hydroxyapatite, whereas biological haemostatic agents include fibrin glue and similar substances.

The outcome of bone grafting was assessed mainly with the Bergland grading system using 2-dimensional radiographs including panoramic, occlusal, and periapical films to measure the height of interalveolar bone.[12,13] Nevertheless, the reliability of the quality of 2-dimensional images for clinical assessment is questionable because of several drawbacks, including the lack of volumetric data, distortion, and problems with magnification while the images are being captured, an overlap of anatomical structures, and the absence of a reliable set of identifiable anatomical landmarks.[13,14] With the recent advancement in medical imaging using computed tomography (CT) and the ease of volumetric reconstruction for computational analysis, the use of 3-dimensional volumetric analysis is becoming more common in the assessment of the outcome of bone grafting.[13,15]

So far two major factors have contributed to the heterogeneity of the assessment of these outcomes: the grafting material used (autogenous or tissue-engineered) and the method of measuring the volume of the cleft before and after operation. We know of no published comprehensive studies that have compared outcomes (for percentage of bone volume filled) of different interventions based on 3-dimensional volumetric measurements. This systematic review and meta-analysis was therefore designed to provide insights into the effectiveness of the two major treatments (autogenous bone from various donor sites and the different tissue-engineering materials). The results of the meta-analysis provide evidence about whether treatment with regenerative bone substitutes yields improved outcomes compared with treatment with autogenous bone grafts.

Material and methods

Study protocol and registration

The study was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Supplemental data, online only).[16] A protocol was established according to the evidence-based PICO model (population, intervention, comparison, and outcome) to answer the following question:

In patients with congenital cleft lip and palate with alveolar cleft defect, what is the effectiveness of different grafting surgical interventions (autogenous or tissue-engineered bone substitutes) in filling the alveolar cleft defect with bone as detected by radiographic volumetric imaging?

The protocol was reviewed by all the authors and subsequently registered in the International Prospective Register of Systematic Reviews, PROSPERO (Registration number CRD42017065045) (Supplemental data, online only).[17]

Sources of information and search strategy

We made a comprehensive search of major online electronic databases, including MEDLINE, EMBASE, SCOPUS, and Web of Science. The search covered published publications listed in each database from its inception to 1 February 2017. No language restriction was applied. Relevant terms and keywords sought included "cleft lip and palate"; "bone grafting"; "maxillary alveolus"; and "transplantation" (Table S1). We also searched "grey" publications (materials and research produced by organisations outside traditional channels for commercial or academic publishing and distribution) and relevant cross references.

Please cite this article in press as: Kamal M, et al. Volumetric comparison of autogenous bone and tissue-engineered bone replacement materials in alveolar cleft repair: a systematic review and meta-analysis. *Br J Oral Maxillofac Surg* (2017), https://doi.org/10.1016/j.bjoms.2018.05.007