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Perspective

# The feasibility of craniofacial-derived bone marrow stem cells for the treatment of oral and maxillofacial hard tissue defects

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The currently available treatment approaches in oral and maxillofacial bone regeneration provide the structural and functional repair of the defect area; nonetheless, many of the treatment modalities entail more improvements to meet the standards concerning the biological aspects of oral and maxillofacial reconstruction. Thus, employing novel strategies of cell-based tissue regeneration can be an alternative approach to evade the current limitations of oral and maxillofacial reconstruction techniques.<sup>1</sup> In this regard, bone

marrow mesenchymal stem cells (BMSCs), as an at-hand source of stem cells, have recently been noticed in bone regeneration of oral and maxillofacial regions.<sup>2–5</sup> Several preclinical studies have verified their promising use for bone regeneration,<sup>6–8</sup> and more recently, various clinical reports have demonstrated their aptitude in the regeneration of oral and maxillofacial defects when used in autologous grafts.<sup>2–5</sup> The distinguishable advantages of BMSCs are their favorable osteogenic potentials, availability, and applicability in comparison to the other sources of stem cells. Considering these features, they can be presumed as a promising source.<sup>4,7,8</sup>

Regularly, oral and maxillofacial surgeons obtain the BMSCs from the iliac crest for treatment of hard tissue defects.<sup>2–5</sup> In this approach, the process of BMSCs extraction

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could be performed several weeks or right before the proposed oral and maxillofacial surgery.<sup>3,5,9</sup> Although various studies exhibited favorable outcomes of administration of BMSCs for treatment of bony defects,<sup>3–5,9</sup> isolation of BMSCs from iliac crest and complications associated with it remain a great challenge that can restrict its application for future clinical settings. The complications associated with harvesting BMSCs from the iliac crest could happen in 1%–25% of instances and include hematoma, seroma, nerve injury, cosmetic deformity, abdominal hernia, pelvic instability ileus, infection, and persistent pain.<sup>10</sup>

Concerning the shortcomings mentioned above, an alternative approach in harvesting BMSCs from other sources might possibly overcome the current limitations. In this regard, several authors<sup>1,11–13</sup> have investigated the applicability of craniofacial-derived BMSCs as an alternative source of BMSCs for bone regeneration in the oral and maxillofacial regions. Given the results of many studies,<sup>11–13</sup> craniofacial-derived BMSCs have exhibited superior osteogenic capability compared to those obtained from the iliac crest, femur, tibia, and so on. Moreover, various techniques are developed to extract a sufficient amount of BMSCs from the alveolar bone.<sup>13</sup> Additionally, since these BMSCs can be easily harvested from alveolar bone with negligible pain to the patients, they may be more valuable for regenerative medicine purposes in comparison to the invasive harvesting of BMSCs from the iliac crest.<sup>13</sup> According to Matsubara et al.,<sup>13</sup> isolating BMSCs from the alveolar bone can be performed during wisdom teeth extractions, jaw deformity osteotomies, dental implant surgeries, trauma surgeries, and cyst removals. Hence, harvesting BMSCs during and throughout the wisdom teeth extractions and jaw deformity osteotomies and employing these resources seem to exhibit the highest success rates in the regeneration of hard tissue defects. This issue is ascribed to the effect of age on the number and function of stem cells since the patients indicated for the mentioned surgeries are usually younger.<sup>13</sup> Moreover, Lloyd et al.<sup>11</sup> have reported a novel method regarding the harvesting of the craniofacial-derived BMSCs. They<sup>11</sup> reported that the labial symphyseal area, i.e., 1 cm distal to the midline, and 1 cm superior to the inferior border of the mandible is a proper location for harvesting approximately 10–18 ml of bone marrow aspirates combined with heparin.

The higher osteogenic capacity and lower adipogenic and chondrogenic capacity of the craniofacial-derived BMSCs compared to its counterparts in the iliac, femoral, and tibial bone marrow<sup>11–13</sup> along with its easier availability and appropriate applicability for the oral and maxillofacial surgeon can be safely pledged for future translational investigations. As mentioned earlier, oral and maxillofacial surgeons, periodontists and other related dental practitioners can isolate craniofacial-derived BMSCs much easier through the routine oral surgical procedures such as tooth extraction, dental implant surgery, distraction osteogenesis initial incision, crown lengthening. This procedure can be performed without the need for any general anesthesia and the secondary site complications

would be the least.<sup>14</sup> Therefore, regarding all the aforementioned advantages, we propose that craniofacial-derived BMSCs can be feasible for the treatment of oral and maxillofacial hard tissue defects as an acceptable alternative to those obtained from the iliac crest. Although currently, the application of stem cells in daily practice is limited, optimizing the current techniques to achieve the best attainable outcome in future translational and clinical investigations is of high importance. Therefore, to confirm the outcomes of current in-vitro studies and spot the present gaps, many standard randomized controlled trials (RCTs) are needed to evaluate the feasibility of craniofacial-derived BMSCs in oral and maxillofacial bone tissue engineering.

## Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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