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Success rate and risk factors of failure of the induced membrane technique in children: a systematic review

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KEYWORDS

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osteosynthesis
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autograft

ABSTRACT

The induced membrane technique was designed by Masquelet et al. to address segmental bone defects of critical size in adults. It has been used after bone defects of traumatic, infectious and tumoral origin with satisfactory results. Recently, it has been used in children but, after an initial enthusiasm, several cases of failure have been reported. The purpose of this study was to assess the success rate and the risk factors of failure of the induced membrane for children.

We conducted a systematic review of all the studies reporting the results of the induced membrane technique to address bone defects of critical size in children. Our primary outcome was the success rate of the technique defined as a bone union before any iterative surgery. Our secondary outcomes were the complications and the risk factors of failure.

We searched Medline via Pubmed, EMBASE and the Cochrane Library. Twelve studies, including 69 patients, met the inclusion criteria. There were 41 boys and 28 girls. Mean age at surgery was 10 years. Mean size of resection was 12.38 cm and the mean time between the two stages was 5.86 months. Mean rate of bone union after the two stages of the induced membrane technique was 58% (40/69) but this rate increased to 87% after revision surgeries (60/69). Main complications were non-unions (19/69), lysis of the graft (6/69) and fractures of the bone graft (6/69). Only 1/69 deep infection was reported. Other non specific complications were regularly reported such limb length discrepancies, joint stiffness and protruding wires. Risk factor of failure that could be suspected comprised the resection of a malignant tumour, a bone defect located at the femur, a wide resection, a long time between the two stages, an unstable osteosynthesis and a bone graft associating autograft to other graft materials.

The induced membrane technique is suitable for bone defects of critical size in children. It is a reliable technique with no need of micro vascular surgery. However, we found several risk factors of failure for the use of the induced membrane technique to address segmental bone defect of critical size in children.

Introduction

Segmental bone defects are rare but dramatic situations in children. They can be a consequence of several diseases such as congenital pseudarthrosis, traumas, bone infection or bone tumours. Yet, only few surgical techniques exist to address segmental bone defects of critical size. Among them, the most reported are the vascularised fibular transplant, the Ilizarov external fixator technique for bone transport and the induced membrane technique [1]. To the best of our knowledge, none of these techniques has proven superiority to the other ones.

The induced membrane technique was described by Masquelet et al. to address bone defects of critical size [2]. It is a two-stage technique involving the insertion of a cement spacer in the bone defect in order to create a protective membrane, and a secondary reconstruction of the bone defect with bone grafting inside the created membrane. This technique presents many advantages such as a relative short time of reconstruction even for large bone defects, a high rate of bone union and a very low rate of complications. Indeed, its efficacy has been reported after bone defects of various origins in adults [2–6]. In children however, it has been reported after defects from traumatic, congenital or tumoral origins with mixed results [7–12].

Hence, it seems that the induced membrane in children may have a different behaviour than the induced membrane in adults. Furthermore, there are probably different factors explaining the successes or failures of this technique among children. Thus, it would be interesting to explore the risk factors of failure of the induced

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membrane technique used to address bone defect of critical size in children. However, given the rarity of the indications of the induced membrane in children, neither a prospective nor a retrospective study in one – or even several – specialized centres would add a sufficient number of clinical cases to allow a good answer to these very important question. That is why the analysis of the data already available in the literature may be the better way to obtain valuable information.

To do so, we designed a systematic review of all the studies reporting the results of the induced membrane technique to address bone defects of critical size in children. Our goal was to identify the success rate, the complications and the factors of failure of the induced membrane technique for children. We hypothesized that the rate of success of the induced membrane technique depended on (1) the initial disease, (2) the distance between the resection and the remaining epiphysis, (3) the stability of the osteosynthesis performed, (4) the type of bone graft used.

Material and methods

Protocol and registration

The objectives, methods of the analysis and inclusion/exclusion criteria for this study were specified in advance and documented in a protocol. This protocol was registered and made publicly available at http://www.crd.york.ac.uk/prospero/search.asp. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used in the design and conduction of the present systematic review [13,14].

Eligibility criteria

Type of study: Studies reporting the results of the induced membrane for bone defects of critical size in children were aimed to be included in this study. Only clinical trials, either prospective or retrospective, published in English or French, without any other restriction in publication, were considered for inclusion. We did not aim to include any abstracts or unpublished material in the analysis.

Type of patient: Only studies concerning children were considered for inclusion. Any cause of critical size bone defect was included: congenital deficiency, post-traumatic non-union, bone infection and primary bone tumour. All the anatomical locations of the bone defect were considered. No study reporting results of the induced membrane technique in adult was included.

Type of intervention: Only studies reporting the results of the induced membrane technique for bone defect of critical size were considered for inclusion in this review. Any type of osteosynthesis and any type of graft were considered. However, other reconstructive techniques such as vascularised fibular transplant, Ilizarov technique or other type of grafts were excluded.

Type of outcome measures: The primary outcome measure was bone union occurring after the second stage of the induced membrane technique and before any iterative surgery. Bone union was assessed on two orthogonal plain radiographs when three corticals were appearing continuous between the two extremities of the bone defect. The secondary outcomes were the complications and the risk factors of failure.

Information sources

Studies were identified by searching MEDLINE via PubMed, EMBASE and the Cochrane library. The last search was run on June 1 2016. The closing date was to be extended in case the retrieval period demanded a significant amount of time so that there would be little risk to exclude relevant and recent studies. We did not attempt to acquire any missing information (*e.g., on study methods or results*) from investigators of the included studies.

Search

The following search terms were used to search the aforementioned databases: *(induced [All Fields] AND ("membranes"[MeSH Terms] OR "membranes"[All Fields] OR "membrane"[All Fields])) AND ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields])*

Study selection

Two authors (*JCA and GR*) performed the eligibility assessment independently in a not blinded standardized manner. First, they reviewed the titles and abstracts resulting from the search. Then, all the studies selected were retrieved and evaluated further from the text to assess the inclusion and exclusion criteria. Finally, the two authors hand searched the references of every included study in order to detect any additional studies meeting the inclusion and exclusion criteria. Any disagreements between reviewers were resolved by consensus. In case a disagreement would persist, a third review by another author (*TB*) would be asked.

Data collection process

We developed a data extraction sheet based on the Cochrane Consumers and Communication Review Group's data extraction template, pilot-tested it on the first three included studies, and refined it accordingly. Two authors (*JCA and GR*) extracted the data from included studies. The authors aimed to avoid the inclusion of multiple reports of the same study by juxtaposing author names, location of the study and sample sizes. When a duplicated study was suspected, only the more recent and/or the more complete was included. Then, the other reports were used to complete any lack of data in the selected study. Disagreements were resolved by discussion between the two review authors. If no agreement could be reached, it was planned a third author (*TB*) would decide. Finally, we did not plan to contact any author to obtain further information from the included studies.

Data items

Information was extracted from each included study on: (1) the characteristics of the participants (date of inclusion, gender, age, initial disease, localization of the defect, size of the defect), (2) the type of interventions (time between the two stages of the technique, type of osteosynthesis, type of graft, adjuvant treatment such as chemo/gamma therapy, post-operative immobilization), (3) the outcome measure (bone union, complications, number of iterative surgeries, cause assumed for the failure). No new variable was added after the final review started.

Risk of bias in individual studies

Because of the expected high rate of descriptive retrospective studies, the risk of bias was evaluated using the STROBE checklist (*Strengthening the Reporting of Observational Studies in Epidemiology*) in order to provide a score of 0–28 for each included study [15]. Although STROBE criteria do not assess the quality of research, they provide a perspective on the quality of reporting that can be useful for the critical appraising published studies [15]. No study has been excluded based on this score.

Summary measures

The primary outcome measure was bone union occurring after the second stage of the induced membrane technique and before any iterative surgery. Bone union was assessed on two orthogonal plain radiographs when three corticals were appearing continuous between the two extremities of the bone defect. The secondary outcomes were