Effect of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps: A meta-analysis

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Abstract
A meta-analysis was performed to evaluate the effect of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps. A systematic literature search until March 2022 incorporated 386 subjects after endoscopic sinus surgery of nasal polyps at the beginning of the study; 187 were using chitosan-based gel dressing, and 199 were control. Statistical tools like the dichotomous method were used within a random or fixed-influence model to establish the odds ratio (OR) with 95% confidence intervals (CIs) to evaluate the influence of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps. Chitosan-based gel dressing had significantly lower wound infection (OR, 0.48; 95% CI, 0.25–0.92, \(P = 0.03\)), and synechia (OR, 0.25; 95% CI, 0.13–0.50, \(P < 0.001\)) compared with control in subjects with endoscopic sinus surgery of nasal polyps. However, no significant difference was found in granulations between chitosan-based gel dressing and control in subjects with endoscopic sinus surgery of nasal polyps. Chitosan-based gel dressing had significantly lower wound infection, synechia compared with control in subjects with endoscopic sinus surgery of nasal polyps, and no significant difference in granulations. Further studies are required to validate these findings.

Keywords
chitosan-based gel dressing, endoscopic sinus surgery of nasal polyps, granulations, synechia, wound infection

Key Messages
• The diabetic foot ulcer wound is a severe problem in subjects with diabetes mellitus.
• A meta-analysis was performed to evaluate the association between vitamin D deficiency and diabetic foot ulcer wounds in diabetic subjects.
Diabetic subjects with foot ulcer wounds had significantly lower vitamin D parameters compared with non-ulcerated diabetic subjects.

Further studies are required to validate these findings.

1 | BACKGROUND

Chronic rhinosinusitis, septal deviation, and inferior turbinate hypertrophy were abundant in clinical practice and can cause persistent nasal obstruction and significantly decreased quality of life. These also may result in anosmia, headache, dizziness, and insomnia. Endoscopic sinus surgery was a vital technique to manage chronic rhinosinusitis, septal deviation, and inferior turbinate hypertrophy when medical management failed but had certain restrictions, comprising postoperative bleeding and synechia (adhesions on the active side at all-time points) formation. Postoperative recovery was influenced by scarring and re-obstruction of the ostiomeatal complex. Nasal packing was described to be one common method to stop postoperative bleeding and endorse wound healing. Conventional removable nasal packing comprised gauze, cotton, and a sponge. For example, Merocel (Medtronic, Inc., Minneapolis, MN, USA), which consists of an expandable polyvinyl acetate sponge, was a typical conventional removable nasal packing and had some benefits, comprising cheap price, easy handling, and adequate supporting capability. Although, conventional removable nasal packing was restricted by some inadequacies, for example, nasal airway blockage; bleeding because of extramucosal disorders; headache and pressure; painful mouth, pharynx dryness, and tremendous anxiety. Chitosan was acquired by alkaline deacetylation of natural chitins and is a good haemostatic agent, with a significant capability to fast clot blood, hypoallergenicity, and antimicrobial influence. Nasal dressing that consists of cross-linking chitosan and dextran derivatives gel was used as a haemostatic agent post-nasal surgery. Earlier studies showed that chitosan-based gel dressing was related to reduced synechia and crustng, and better wound healing post-endoscopic sinus surgery. However, some relevant randomised controlled trials showed that chitosan gel dressing has no influence on synechia, granulations, crustng, and wound infection. Thus, we performed this meta-analysis of randomised controlled trials to evaluate the effectiveness of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps.

2 | METHODS

A methodology was established according to the epidemiology statement which is further organised into a meta-analysis.

2.1 | Study selection

The main indications of the meta-analysis were to assess the effect of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps using statistical tools like mean difference (MD), odds ratio (OR), frequency rate, or relative risk at a 95% confidence interval (CI).

The literature review was limited to the English language. However, inclusion criteria were not restricted by study type or size, and studies with no relationships were excluded from the study, for example, letters, editorials, commentary, and review articles. Figure 1 represents the model of meta-analysis.

Inclusion criteria of the analysis incorporated into the meta-analysis are given below.

1. The studies were prospective studies, randomised control trials, or retrospective studies.
2. Subject selected for the study was subjects after endoscopic sinus surgery of nasal polyps.
3. Chitosan-based gel dressings were considered as intervention programs.
4. The study comprised chitosan-based gel dressing, compared with control.

The exclusion criteria adopted for the analysis were

1. Studies that do not assess the effects of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps.
2. Studies with management other than chitosan-based gel dressing.
3. Studies that do not influence comparative outcomes.

2.2 | Identification

Search strategy adopted the protocol as the PICOS principle the critical elements of PICOS were P (population): subjects after endoscopic sinus surgery of nasal polyps; I (intervention/exposure): chitosan-based gel dressing; C (comparison): chitosan-based gel dressing compared with control; O (outcome): wound infection, synechia, and granulations S (study design): without any limitation. A systematic and brief literature survey was performed on MEDLINE/PubMed, Google
Scholar, Embase, OVID, Cochrane Library, and until March 2022, using search keywords like chitosan-based gel dressing, granulations, wound infection, synechia, and endoscopic sinus surgery of nasal polyps as depicted in Table 1. The research papers were arranged using EndNote software to exclude the duplicates. Moreover, a rigorous analysis of all title and abstracts were carried out to delete any data that did not indicate any risk factors or impact of chitosan-based gel dressing on the outcomes studied. Related Information on this topic was collected from the remaining topics.

2.2.1 | Screening

A standard format was established, including the study and subject-related data. In addition, a traditional form was categorised to include the first author’s surname, place of practice, duration of the study, design of the study, sample size, subject type, demography, categories, treatment mode, qualitative and quantitative evaluation, information source, primary outcome evaluation, and statistical analysis.18

“Risk of bias tool” was adopted to assess the methodological quality using Cochrane Handbook for Systematic Reviews of Interventions Version 5.1. To ensure the quality of the methodology, the corresponding author resolved any conflicts through a discussion that arose during the collection of literature by two reviewers.19

| Database          | Search strategy                                                                                                                                 |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| Pubmed            | #1 “chitosan-based gel dressing”[MeSH Terms] OR “endoscopic sinus surgery of nasal polyps”[MeSH Terms] OR “synechia”[All Fields] #2 “granulations”[MeSH Terms] OR “wound infection”[All Fields] #3 #1 AND #2 |
| Embase            | ‘chitosan-based gel dressing’/exp OR ‘endoscopic sinus surgery of nasal polyps’/exp OR ‘synechia’/exp #2 ‘granulations’/exp OR ‘wound infection’/exp #3 #1 AND #2 |
| Cochrane library  | #1 (chitosan-based gel dressing):ti,ab,kw OR (endoscopic sinus surgery of nasal polyps):ti,ab,kw (Word variations have been searched) #2 (granulations):ti,ab,kw OR (wound infection):ti,ab,kw (Word variations have been searched) #3 #1 AND #2 |
2.3 The different levels of risk of bias encountered in assessment criteria

In the assessment of criteria, there are three different levels of risk of bias. The bias is considered low risk when all quality parameters were met; moderate risk when parameters were only partially completed or not met; It is regarded as a high-risk bias when all quality parameters were not met/or not included. Inconsistencies are checked by examining the paper.

2.4 Eligibility criteria

The effect of chitosan-based gel dressing on wound infection, synechia, and granulations was considered the study’s eligibility criteria. Therefore, an evaluation of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps compared with control was extracted to form a summary.

2.5 Inclusion criteria

This sensitivity analysis included only the effect of chitosan-based gel dressing after the endoscopic sinus surgery of nasal polyps compared with control. In comparison, the sensitivity analysis subcategory had the chitosan-based gel dressing compared with the control.

2.6 Statistical analysis

The statistical analysis adopted a dichotomous method to calculate the odds ratio (OR) at a confidence interval (CI) of 95% on the random influence or fixed influence model. Initially, the $I^2$ index scale was assessed between 0% and 100%, and the scale for heterogeneity was set between 0%, 25%, 50%, and 75%, which indicated scales as no, low, moderate, and high, respectively. If $I^2$ was 50%, the random influence was considered, and if $I^2 < 50\%$, it was regarded as fixed-influence. Initial results are pooled, and subgroup analysis was performed to get a $P$-value that is statistically significant $<0.05$. The Egger regression test assesses publication bias (if $P \geq 0.05$) by calculating funnel plots of the logarithm of odds ratios compared with standard errors. The statistical analysis was performed by “Reviewer manager version 5.3”. (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) with two-tailed $P$ values.

3 RESULTS

A total of 6 studies reported between 2010 and 2022 satisfied the inclusion criteria for the meta-analysis among the 546 distinctive reports. This meta-analysis study included 386 subjects after endoscopic sinus surgery of nasal polyps at the beginning of the study; 187 were using chitosan-based gel dressing, and 199 were control. All studies evaluated the effect of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps. 4 studies reported data stratified to the wound infection, 5 studies reported data stratified to the synechia, and 3 studies reported data stratified to the granulations. Most of the studies were done in Austria. 38 to 100 subjects were involved as a study sample size in the selected studies. All information about these 6 studies is given in Table 2.

Chitosan-based gel dressing had significantly lower wound infection (OR, 0.48; 95% CI, 0.25–0.92, $P = 0.03$) with low heterogeneity as $I^2 = 39\%$, and lower synechia (OR, 0.25; 95% CI, 0.13–0.50, $P < 0.001$) with heterogeneity denoted as low ($I^2 = 49\%$) compared with control in subjects with endoscopic sinus surgery of nasal polyps as shown in Figures 2–3. However, no significant difference was found in granulations between chitosan-based gel dressing and control in subjects after endoscopic sinus

| Study          | Country    | Total | Chitosan | Control |
|---------------|------------|-------|----------|---------|
| Valentine, 2010 | Australia  | 80    | 40       | 40      |
| Ngoc Ha, 2013  | New Zealand| 52    | 26       | 26      |
| Chung, 2016    | Korea      | 66    | 33       | 33      |
| Ha, 2018      | Australia  | 38    | 13       | 25      |
| Khafagy, 2021  | Qatar      | 100   | 50       | 50      |
| Megow, 2022   | Australia  | 50    | 25       | 25      |
| **Total**     |            | 386   | 187      | 199     |
surgery of nasal polyps (OR, 1.57; 95% CI, 0.49–5.00, \( P = 0.45 \)) with no heterogeneity as \( I^2 = 0\% \) as shown in Figure 4.

The pooled data has not considered the elements like group age, ethnicity, and gender because of the lack of reports on these elements. The results of Egger regression analysis funnel plots during the quantitative measurement have not proved any publication bias (\( P = 0.89 \)). However, problems like poor methodological tools were identified in the selected randomised dressings-led trial. Selective reporting bias was not detected during this meta-analysis.

### DISCUSSION

This meta-analysis comprised 386 subjects after endoscopic sinus surgery of nasal polyps at the beginning of the study; 187 were using chitosan-based gel dressing, and 199 were control.\(^{10-15} \) Chitosan-based gel dressing had significantly lower wound infection, and synechia compared with control in subjects with endoscopic sinus surgery of nasal polyps. However, no significant difference was found in granulations between chitosan-based gel dressing and control in subjects with endoscopic sinus surgery of nasal polyps. Yet, the analysis of results must
be performed with attention due to the low number of selected studies and the low sample size of all the selected studies found for the meta-analysis, 6 out of 6 studies with ≤100 subjects as sample size; recommending the necessity for additional studies to confirm these findings or perhaps to significantly impact confidence in the effect assessment.

The main aim of this meta-analysis was to show and assess all current indications about the effect of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps. Conventional packing, for example, ribbon gauze and Merocel, are commonly used removable materials.21 Alteration with chemicals or glove fingers can partially improve postoperative results. Gloved Merocel (Medtronic, North Haven, CT, USA) was shown to improve the pain at packing removal.21 Although, numerous problems, for example, septal perforation, aspiration, toxic shock syndrome, foreign body granuloma, obstructive sleep apnea (secondary to nasal obstruction), and even mortality, have stopped conventional packing prevalent usage in clinical practice.21 Numerous biodegradable products, for example, NasoPore, Cutanplast (Mascia Brunelli Spa, Milano, Italy), hyaluronic acid, and carboxymethylcellulose, were industrialised to function as nasal packing.22 Biodegradable packing was shown to improve adequate haemostasis by easing water uptake or motivating clotting.23 Their dissolution happened in a couple of days. Biodegradable packing gave a better quality of life through the early recovery time than conventional packing.24 Chitosan as a natural polymer was produced from chitin25 and has been used as an antimicrobial coating on fruits and vegetables, a coating for seeds before planting, and a hydrating cosmetic product.26 Chitosan-based gel dressing has arisen as a progressively essential selection after endoscopic sinus surgery. Throughout mucosal healing, synechia creation was one of the most frequent post-endoscopic sinus surgery problems and commonly happened between the middle turbinate and the lateral nasal walls. Degradable packing can isolate two mucosal surfaces in the middle meatus and ease the early wound-healing procedure break.27 In addition, a significantly higher fraction of reepithelialization was shown when using chitosan-derivative gel after endoscopic sinus surgery in a sheep model.28 Postoperative bleeding was one serious problem of endoscopic sinus surgery. Significant post-endoscopic sinus surgery haemorrhage might be infrequent, but some degree of epistaxis can happen post-operatively in a few days after surgery and can cause significant anxiety and a negative influence on the recovery process.29 There were some worries concerning the requirement of extra packing for endoscopic sinus surgery and septoplasty to stop bleeding.30 The results of our meta-analysis show that chitosan does not increase wound infection. That would make its use safer for such patients. However, no significant difference was found in the granulations. That was observed because of the low number of studies found. This study exhibited a correlation between the effects of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps. However, more trials are still required to explain the exact clinical difference in the results and closeness. Moreover, to study the elements with the group age, ethnicity, and gender; our meta-analysis studies could not prove these factors are related to the outcomes. This was suggested in other meta-analyses, which showed similar effects31-33; to the level that one study included data from the sheep’s model to have a rational result because they could not find enough data from human studies.31 In summary, chitosan-based gel dressing had significantly lower wound infection, lower synechia compared with control in subjects with endoscopic sinus surgery of nasal polyps, and no significant difference in granulations.

4.1 | Limitations

One of the study’s limitations was various biases existed as many studies were exempted from this meta-analysis as these studies were not meeting the inclusion criteria. Furthermore, there was an uncertainty in linking the factors like gender, age, and ethnicity to this analysis. The study compared the correlation of the influences of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps. The analysis depends on data from existing studies which can result in bias as it contains incomplete details. The meta-analysis consisted of 6 studies; 6 of them were small, ≤ 100. Several lost data and unpublished studies may aggregate into an influence bias. Patients used various medications, health care schemes, treatments, and doses. And also, the type of dressing of the included studies varied.

5 | CONCLUSIONS

Chitosan-based gel dressing had significantly lower wound infection, lower synechia compared with control in subjects with endoscopic sinus surgery of nasal polyps, and no significant difference in granulations. Yet, the analysis of results must be performed with attention due to the low number of selected studies and the low sample size of all of the selected studies found for the meta-analysis, recommending the necessity for additional studies to confirm these findings or perhaps to significantly impact confidence in the effect assessment.
DATA AVAILABILITY STATEMENT
The corresponding author is bound to give the database of meta-analysis on request.

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