

Complications of Urethral Bulking Agents for Stress Urinary Incontinence: An Extensive Review including Case Reports

Allert de Vries¹, MD, Harpreet Wadhwa², MD, Jason Huang², MD, Fawzy Farag³, MD, PhD, John Heesakkers¹, MD, PhD, Ervin Kocjancic², MD
¹ Department of Urology - Radboud University Medical Centre, Nijmegen, The Netherlands; ² Department of Urology – University of Illinois, Chicago, USA; ³Department of Urology, Sohag University Hospital, Sohag, Egypt

Introduction

There is much literature describing the clinical results of -often newly introduced- urethral bulking agents, however there is a lack of high-quality comparative articles. These publications however are used for conventional systematic reviews, disregarding a large portion of published data. The aim of this study was therefore to perform an extensive review of all available literature, **including case reports**, to get a broader view of the complications encountered with the recently available bulking agents.

Methods

On March 7, 2016, we performed an **extensive search** in the PubMed, Embase and Cochrane databases. The search was limited to the synonyms or equivalents of “urethra,” “urinary incontinence,” and the different bulking agents. All original articles and case reports describing the complications of urethral bulking agents were included, regardless of the methodological quality.

Results

Treatment of complications per product in original articles

| | No of treated patients | Total no of complications | Non-invasive Management | Incision & drainage | Invasive surgery | No of Clavien III complications |
|----------------|------------------------|---------------------------|-------------------------|---------------------|------------------|---------------------------------|
| Bulkamid | 1052 | 189(18%) | 188 | 0 | 1 | 1(0.00%) |
| Coaptite | 141 | 64(45%) | 63 | 0 | 1 | 1(0.01%) |
| Contigen | 3173 | 690(22%) | 688 | 0 | 2 | 2(0.00%) |
| Durasphere | 326 | 80(25%) | 76 | 3 | 1 | 4(0.01%) |
| Macroplastique | 654 | 620(95%) | 620 | 0 | 0 | 0(0.00%) |
| Tegress | 156 | 21(13%) | 20 | 0 | 1 | 1(0.01%) |
| Urolastic | 127 | 31(24%) | 17 | 2 | 12 | 14(11.02%) |
| Zuidex | 833 | 400(48%) | 356 | 41 | 3 | 44(5.28%) |
| Total | 6462 | 2095(32%) | 2028 | 46 | 21 | 67(1.04%) |

Noninvasive management: includes watchful waiting/antibiotics/CIC/suprapubic tube

invasive surgery: includes excision/reconstruction

Original articles

In **6462 treated patients** a total of **2095 complications (32%)** were reported in the **79 analyzed studies**. Of the reported complications, **67 (3%)** were considered major (Clavien Grade III - requiring an additional procedure). The remaining 2028 complications were treated with conservative therapy.

Treatment of complications from case reports

| | No of complications | Non-invasive Management | Incision & drainage | Invasive surgery |
|----------------|---------------------|-------------------------|---------------------|------------------|
| Bulkamid | 1 | 0 | 1 | 0 |
| Coaptite | 5 | 0 | 2 | 3 |
| Contigen | 23 | 7 | 5 | 11 |
| Durasphere | 5 | 1 | 1 | 3 |
| Macroplastique | 4 | 0 | 0 | 4 |
| Tegress | 2 | 2 | 0 | 0 |
| Urolastic | 0 | 0 | 0 | 0 |
| Zuidex | 10 | 0 | 7 | 3 |
| Total | 50 | 10 | 16 | 24 |

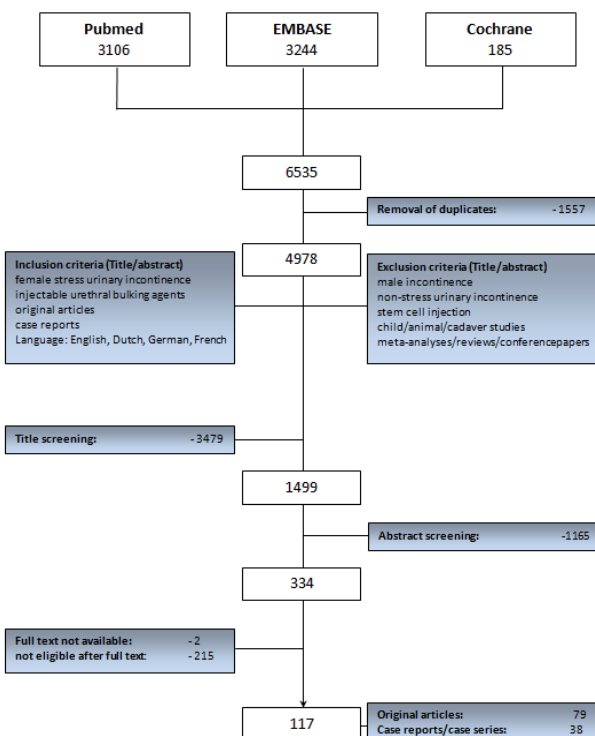
noninvasive management: includes watchful waiting/antibiotics/CIC/suprapubic tube

invasive surgery: includes excision/reconstruction

Case reports

In **38 case reports** and small case series, **50 patients** were treated for **50 complications**. The complications tend to be more severe, as minor complications are less interesting to report in case reports. Reported treatments are also more invasive than in the original studies. Out of 50 complications, **30 (60.0%)** were classified as Clavien Grade III.

Flowchart



Discussion

The advantage of our method is that many articles were included that would be excluded in standard reviews. After assessment, **only 7 RCT's** described complications and **4 comparative studies**. The remaining 68 articles, with **49 prospective single-arm studies would have been deleted**. This shows that an important part of literature is neglected in systematic reviews. By adding the case-reports another 38 articles were added to the review. **Case reports are an important way to communicate specific concerns about products in medical literature.**

Conclusion

- Bulkamid, Contigen, Durasphere, Tegress and Urolastic have the lowest overall complication rates
- Complications requiring surgical removal were mostly seen with Urolastic and Zuidex
- Despite the limitations, we can conclude that most bulking agents currently available seem to be safe
- Comparison based on efficacy should point out which has the best balance between efficacy and complications

CONTACT INFORMATION

A.M. de Vries, MD PhD-candidate allert.devries@radboudumc.nl
 This study was supported by an unrestricted grant from Urogyn B.V.