

# BOTULINUM TOXIN TYPE A (BTA) INJECTION FOR CHRONIC ANAL FISSURE

## Executive Summary

[Adapted from the report by MAHARITA AB RAHMAN]

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### Background

Anal fissure is an ulcer in the squamous epithelium of the anus located just distal to the muco-cutaneous junction and usually in the posterior midline. It will be considered as acute if the anal fissure present for less than six weeks, superficial and have well-demarcated edges. The anal fissure is considered chronic if they have been present for more than six weeks and have keratinous edges. This technology review (TR) report will highlight the chronic anal fissure (CAF) instead of acute anal fissure (AAF).

Chronic anal fissures typically occur in the midline, with visible sphincter fibres at the fissure base, anal papillae, sentinel piles and indurated margins. Typically, CAF have a cyclical history of intermittent healing and recurrence, but about 35% will eventually heal, at least temporarily, without intervention. The exact pathogenesis of primary fissures remains uncertain, but a core point is hypertonicity of the internal anal sphincter, which leads to local ischaemia. Furthermore, inflammation and pain induce ongoing hypertonicity, giving rise to a vicious circle. Therefore, the aim of treatment strategies is to reduce the sphincter tone with either medical agent such as glyceryl trinitrate (GTN), calcium channel blockers (CCB) and botulinum toxin A (BTA), or surgical interventions such as lateral internal sphincterotomy (LIS). However, there are various approaches that combined either surgical with medical treatment inclusive of BTA or surgical alone as well as medical treatment alone. The efficacy and effectiveness of either surgical alone, medical alone or combination varied

### Objectives

To assess the safety, efficacy or effectiveness and cost-effectiveness of botulinum toxin A (BTA) injection for CAF

### Methods

Electronic databases were searched through Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, EBM Reviews-Cochrane Database of Systematic review, EBM Reviews-Cochrane Methodology Register of Controlled Trials, EBM Reviews-Health Technology Assessment, EBM Reviews-NHS Economic Evaluation Database, and Embase 1996 to 17 8 Jun 2018. Searches were also run in PubMed, FDA website and INAHTA for any published reports.

No limit in the study year. Google and Google Scholar were also used to search for additional web-based materials and information about the technology. Besides, additional articles were also search by reviewing the references of retrieval articles.

### Results and Conclusions

The included studies consisted of three SRs and meta-analysis, one SR and network meta-analysis, one SR, five pre- and post- intervention studies, one non-RCT and one cost analysis study.

### Efficacy / Effectiveness

- Combination of BTA and fissurectomy for CAF showed an improvement in CAF
- LIS surgery was more effective in healing and preventing recurrence of anal fissure compared with BTA but incontinence was lesser with BTA compared with LIS
- There was no significant difference in healing, recurrence rate and incontinence rate among BTA injection and topical nitrates

- BTA injection was significantly more effective than lidocaine
- Different doses of BTA, different injection sites and different types of BTA formulation, did not significantly affect the efficacy and effectiveness of BTA injection for CAF treatment

### **Safety**

- Common complication in the combination treatment was anal bleeding that resolved spontaneously few days after treatment
- Other reported complications that occurred after combination treatment were perianal sepsis, recurrence anal fissure, pruritus ani, delayed healing, and headache
- Comparing BTA injection with topical nitrates, there was more significant complications especially headache occurred in topical nitrates group compared to BTA injection
- The systematic reviews reported BTA injection had low frequencies of adverse events which were mostly local post-operative complications such as hematoma, perianal thrombosis, perianal abscess and temporary incontinence that consisted of liquid and faeces
- One case of fourniere gangrene was reported in patient with diabetes mellitus
- Contraindications included hypersensitivity case, pregnancy, neurological disease including myasthenia, Lambert Eaton Syndrome and Amyotrophic lateral sclerosis and co-administration with amino-glycosides may enhanced the action of BTA

### **Cost**

- No local cost analysis was retrieved on the management of CAF with BTA injection
- One cost analysis from United State of America showed that combination of treatment (BTA injection and surgery for any fail BTA case) was cost saving compared to only surgery (LIS) approach

### **Recommendation**

Botulinum toxin type A injection for chronic anal fissure is recommended for selective patients.