

## A Hospital-Based Assessment of the Beneficial Impact of Probiotics Oral Supplementation on Patients Affected by Chalazion

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### Abstract

**Aim:** The aim of the present study was to define the possible beneficial impact of probiotics oral supplementation on patients affected by chalazion

**Methods:** The study was conducted in the Department of ophthalmology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India for the period of one year. Total 24 enrolled patients underwent a complete ophthalmologic examination, including the assessment of size, duration and location of the chalazion before the recruitment.

**Results:** The trial was accomplished by all the participants. The mean age was matched in the two considered groups ( $P=0.74$ ). Both groups had comparable baseline characteristics in terms of location, size and duration of the chalazion, with the exception of the sex; in fact, there was a higher prevalence in the female. The medical treatment with or without probiotics supplementation was effective only on the small size chalazia. Medium and large size chalazia did not respond to medical treatment with or without probiotics supplementation over the follow-up period (3mo).

**Conclusion:** The considerable difference in time taken for complete resolution of small chalazia between the two groups in favor of the experimental one confirms the presence of a gut-eye axis.

**Keywords:** Microbiome, Probiotics, Chalaziosis, Adults.

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### Introduction

Chalazion is one of the most common inflammatory eyelid lesions diagnosed in ophthalmology, due to a block in the efflux from an oil gland. [1] It appears as a small lipogranulomatous tender swelling. [2] Although the chalazion size is generally less than 1 cm, its dimension will often vary over time; moreover, a small percentage of the chalazia can remain for weeks or months in the lid, as a

non-tender lump. [3] Multiple factors are claimed in the pathogenesis of chalazion and, among these, constitutional atopic and seborrheic, hormonal, immunological, presence of irritable bowel disease, iatrogenic [4,5], infectious, mainly related to *Staphylococcus aureus* and *Cutibacterium acnes*, demodicosis (demodex mite infestation) [6],

dysmetabolic factors such as vitamin A deficiency and diabetes. [7-9]

The treatment options for chalazia vary from conservative methods (eyelid hygiene, warm compresses, topical medications, i.e., antibiotic, corticosteroid or antibiotic corticosteroid combinations) to invasive methods (intra-lesion steroid injection and surgical incision and curettage). When the initial conservative methods fail, intralesional corticosteroid injections or incision and curettage to excise the lesion are performed. Conservative methods offer the lowest complication rate accompanied by a small success. Contrarily, invasive methods are the more effective, even if they exhibit the highest possibility of complications. In fact, the intralesional injection may be complicated by ocular penetration of steroids, subcutaneous fat atrophy and topical depigmentation, retinal and choroidal vascular occlusion (rarely), anterior segment ischemia, intraocular pressure (IOP) elevation, visual loss [10], whereas surgical incision and curettage risks include pain, bleeding, and scarring. [11]

Moreover, it is well known that any eating disorder, such as the excessive intake of saturated fats, can result in a change in the lipid composition secreted by the meibomian glands, decreasing its fluidity. Therefore, it becomes difficult to excrete glandular secretions, leading to chalazia formation. The treatment options for chalazia vary from conservative methods (eyelid hygiene, hot compresses (HC), topical medications, i.e., antibiotic, corticosteroid or antibiotic corticosteroid combinations) to invasive methods (intra-lesion steroid injection and surgical incision and curettage) [12]. When using HC alone, reported resolution rates range from 25 to 50% (Perry & Serniuk 1980) [13]. If initial conservative methods fail to resolve a chalazion, practitioners use intralesional corticosteroid injections or

incision and curettage (I&C) to excise the lesion.

Contrarily, invasive methods are the more effective, even if they exhibit the highest possibility of complications. In fact, the intralesional injection may be complicated by ocular penetration of steroids, subcutaneous fat atrophy and topical depigmentation, retinal and choroidal vascular occlusion (rarely), anterior segment ischemia, intraocular pressure (IOP) elevation, visual loss [14], whereas surgical incision and curettage risks include pain, bleeding, and scarring. [15]

The aim of this study was to verify whether oral specific probiotics can alter the clinical course of chalaziosis and its recurrence.

### Material & Methods

The study was conducted in the Department of ophthalmology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India for the period of one year. Total 24 enrolled patients underwent a complete ophthalmologic examination, including the assessment of size, duration and location of the chalazion before the recruitment.

#### Inclusion criteria:

1. History of sudden onset of painful inflamed mass with an unchanged size for more than 2mo;
2. Location and clinical aspect of the lesion.

#### Exclusion criteria:

1. Presence of an infection of eyelids;
2. Nonpalpable chalazion;
3. Chalazion duration <1mo;
4. Pregnancy;
5. Suspicion of malignancy;
6. Comorbidities such as systemic hypertension, diabetes, chronic intestinal diseases and hormonal or cutaneous imbalances infections mostly due to demodex mite infestation, *S.*

*aureus* and *Cutibacterium acnes*, vitamin A deficiency and personal habits (smoking, eating disorders, etc.).

This prospective comparative pilot study was performed on 24 patients (9 males and 15 females, age range 39-54y, randomly divided into two groups (group A and group B). The group A consisted of 12 patients (5 males and 7 females) who received conservative treatment with tobramycin/dexamethasone ointment for at least 20d combined with the use of warm compression and lid hygiene. The group B comprised 12 patients (4 males and 8 females). In addition to the conservative treatment, group B patients, received a mixture of probiotic microorganisms once a day for up to 3mo. According to their size chalazia were classified in large ( $\geq 4$  mm), medium ( $\geq 2$  to  $< 4$  mm) and small ( $< 2$  mm).

When conservative treatment (with and without probiotics supplementation) failed to resolve the lesion, invasive methods were used, and specifically intralesional steroid injection in medium size chalazion and surgical incision and curettage for the largest, according to the technique described by Nabie *et al.* [14] A single dose of the active probiotic product was packaged in a sachet and consisted of a powder of  $\geq 1 \times 10^9$  live bacteria of *Lactococcus lactis* LLC02 (DSM 29536),  $\geq 1 \times 10^9$  live bacteria of *Lactobacillus delbrueckii* subsp. *bulgaricus* (DSM 16606) and  $\geq 1 \times 10^9$  live bacteria of *Streptococcus thermophilus* ST10 (DSM 25246), and the bulking agent was maltodextrin (Probiotal S.p.A., Novara, Italy). Participants were advised to dissolve the powder in water or milk and to drink it once a day. The active probiotic mixture

consisted of probiotic strains used in food supplement formulations which are commercially available. Flow-cytometry (ISO 19344:2015 IDF 232:2015, results  $> 3 \times 10^9$  AFU) was used to study materials (Biolab Research S.r.l., Novara, Italy) and plate count method was used to confirm target cell count (Biolab Research Method 014-06, results  $> 3 \times 10^9$  CFU). In order to ensure that minimum cell counts were maintained shelf-life was monitored. Moreover, unused sachets restored from the study were tested for their viability using AFU/CFU methods. With rare exceptions, the viability went beyond the minimum dosage essential across the study. Patients of group B were informed to keep the probiotic mixture in a refrigerator at 2°C-8°C.

### Statistical Analysis

Continuous variables were shown as mean  $\pm$  standard deviation (SD) and 95% confidence interval (95%CI). Absolute frequencies and percentages [n (%)] were used to present categorical variables. Associations between categorical variables and groups (group A vs group B) were performed by the  $\chi^2$  test or Fisher's exact test when appropriate. The Shapiro-Wilk test was used to verify the normality of the distribution of continuous variables. Comparisons between group A vs group B and continuous variables (age and time of resolution) were analyzed by Student's t-test. The Cochran-Armitage exact test for trend was using to verify the association between chalazion size and groups. A  $P < 0.05$  was considered statistically detectable. Statistical analysis was performed using SAS version 9.4 and JMP PRO version 15.1 (SAS Institute, Cary, NC, USA).

### Results

**Table 1: Differences in baseline and outcome between the two groups**

Characteristics	Group A	Group B	P
Sex (F/M)	7/5	8/4	1.00
Age, mean $\pm$ SD (95%CI), y	47.90 $\pm$ 3.48 (45.41 to 50.39)	48.60 $\pm$ 5.58 (44.61 to 52.59)	0.74

Laterality (unilateral/bilateral)	6/6	5/7	1.00
<b>Chalazion size (mm)</b>			
Small (<2)	5	4	
Medium ( $\geq 2$ to <4)	5	6	
Large ( $\geq 4$ )	2	2	
Recurrence	0	0	

The trial was accomplished by all the participants. The mean age was matched in the two considered groups ( $P=0.74$ ). Both groups had comparable baseline characteristics in terms of location, size and duration of the chalazion, with the exception of the sex; in fact, there was a higher prevalence in the female. The

medical treatment with or without probiotics supplementation was effective only on the small size chalazia. Medium and large size chalazia did not respond to medical treatment with or without probiotics supplementation over the follow-up period (3mo).

**Table 2: Absolute frequencies of adverse events between the two groups**

Adverse effects	Group A	Group B
Diarrhea	0	1
Constipation	1	0
Appetite loss	1	2
Increased appetite	1	1
Skin rash	1	0
Ocular discomfort	4	4

The treatment did not induce complications in any of the groups. No recurrence of chalaziosis was registered in the two groups.

### Discussion

Chalazion is a localized chronic granulomatous inflammation following blockage of the meibomian glands, more commonly affecting the upper eyelids. The range of presentation can be from a benign, self-limiting nodule to a painful lid swelling complicated by corneal astigmatism and mechanical ptosis from the space-occupying effect of the chalazion in the relatively limited eyelid space. [16] Chalazia are initially managed conservatively using warm compress and antibiotic eye ointment for the prevention of secondary bacterial infection. For persistent lesions, incision and curettage (I&C), steroid injection, or carbon dioxide laser treatment may be considered. [17,18]

The International Workshop on Meibomian Gland Dysfunction defines

chalazion as a condition with localized Meibomian gland dysfunction. [19] Histopathologically, chalazion is a lipogranulomatous reaction caused by liberated lipid. A connective tissue impermeable pseudocapsule is often present around the lesion, especially in those largest and oldest, where fibrosis easily occurs. [20] Any eating disorder, such as an over intake of saturated fats, can make the secretion of Meibomian glands less fluid. So, it becomes hard to spill the glandular secretion leading to chalazia formation. In small size lesions meibomian gland ducts, although with a reduction in flow, still work, allowing resolution through conservative treatment (antibiotic ointment containing steroid and warm compresses). Several pieces of evidence indicate that the microbiome of the ocular surface has potent immune-regulatory functions, and it is relevant in the physiologic preservation of healthy eyes and in the pathogenesis of ocular diseases. [21]

Currently several studies shown that the microbiome of different areas of the body are implicated in the pathophysiology of specific ophthalmic diseases, such as the oral microbiome and glaucoma, together with the intestinal microbiome and uveitis. [22] The different confined microbiomes are indeed linked among them through noncoding small RNAs (miRNAs) signaling activity. MicroRNAs are crucial epigenetic regulators implicated in pathologic signaling and have been found extracellularly in different body fluids. They act in a post-transcriptional fashion, playing a critical role in several biological events. Recently, Rizk and Tüzmen [23] claimed a possible cross-talk between miRNAs and the microbiota. Supporting evidence of miRNAs has already been underlined in some latest studies. [24] Interestingly, altered serum levels of miRNA-223 have been linked to microbiota dysbiosis and an upregulation of miRNA-223 was detected in the autoimmune uveoretinitis rat model. [25]

The supplementation of probiotics was composed of a mixture of live cells of *Lactococcus lactis*, *Streptococcus thermophilus* and *Lactobacillus delbrueckii* subsp. *bulgaricus*, which are the most known microorganisms used. They are Gram-positive, anaerobic bacteria and several types produce not only lactic acid but also other antimicrobial substances, such as hydrogen peroxide and bacteriocins (ribosomal synthesized antimicrobial peptides with bactericidal effects). [26] Lastly, the probiotics supplementation has proved to be safe and effective, in fact, there were no side effects related to their use. The lack of efficacy on medium and large size lesions could be due to their histopathologic characteristics, namely to the presence of the connective tissue impermeable pseudocapsule<sup>10</sup>, which isolates the lesion from the systemic context and therefore makes it only treatable with an invasive approach. Probably, the study conducted on

chalaziosis in children gave more consistent results both for the type and size of the lesion and for a greater ease of action on the modulation of the microbiome. [27,28]

### Conclusion

In conclusion, oral probiotics supplementation is able to have a favorable impact on the clinical course of one of the commonest eyelid disorders, at least for the small size lesions, without inducing remarkable complications. Further studies are needed to confirm this first pilot trial.

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