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Interventions for acute internal hordeolum

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DECLARATIONS OF INTEREST
None.

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Abstract

Background—Hordeolum is a common, painful inflammation of the eyelid margin that is usually caused by bacterial infection. The infection affects oil glands of the eyelid and can be internal or external. In many cases, the lesion drains spontaneously and resolves untreated; however, the inflammation can spread to other ocular glands or tissues, and recurrences are common. If unresolved, acute internal hordeolum can become chronic or can develop into a chalazion. External hordeola, also known as styes, were not included in the scope of this review.

Objectives—The objective of this review was to investigate the effectiveness and safety of nonsurgical treatments for acute internal hordeolum compared with observation or placebo.

Search methods—We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (*The Cochrane Library* 2012, Issue 7), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE, (January 1950 to July 2012), EMBASE (January 1980 to July 2012), Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to July 2012), the *meta*Register of Controlled Trials (*m*RCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 26 July 2012.

Selection criteria—The selection criteria for this review included randomized or quasi-randomized clinical trials of participants diagnosed with acute internal hordeolum. Studies of participants with external hordeolum (stye), chronic hordeolum, or chalazion were excluded. Nonsurgical interventions of interest included the use of hot or warm compresses, lid scrubs, antibiotics, or steroids compared with observation, placebo, or other active interventions.

Data collection and analysis—Two review authors independently assessed the references identified by electronic searches for inclusion in this review. No relevant studies were found. The reasons for exclusion were documented.

Main results—No trials were identified for inclusion in this review. Most of the references identified from our search reported on external hordeola or chronic internal hordeola. The few references specific to acute internal hordeolum reported mostly recommendations for treatment or were reports of interventional case series, case studies, or other types of observational study designs and were published more than 20 years ago.

Authors' conclusions—We did not find any evidence for or against the effectiveness of nonsurgical interventions for the treatment of hordeolum. Controlled clinical trials would be useful in determining which interventions are effective for the treatment of acute internal hordeolum.

INDEX TERMS: Medical Subject Headings (MeSH)

Acute Disease; Hordeolum [pathology; *surgery]

MeSH check words

Humans

PLAIN LANGUAGE SUMMARY

Interventions for acute internal hordeolum

Hordeolum is a common, painful inflammation of the eyelid that is usually caused by a bacterial infection. The infection affects the oil glands in the eyelid and results in a lump. Often, the infected lump drains and heals by itself with no treatment. However, the infection can sometimes spread to other glands in the eyes and can become long lasting. It can also turn into a cyst (known as a chalazion).

Hordeolum can be internal (on the inside of the eyelid) or external (on the outside of the eyelid near the eyelashes). Hordeolum on the outside of the eyelid is known as a stye. Hordeolum also can be acute (appearing suddenly and healing in a short time) or chronic (long lasting and occurring over time).

Common treatments for hordeolum include warm compresses applied at home, available over-the-counter topical medications and lid scrubs, antibiotics or steroids, lid massages, and others. The purpose of this review was to see whether these treatments work. We included only studies of patients with acute internal hordeolum. We did not include studies of patients with styes or long-lasting cases of hordeolum.

We identified no trials for this review, thus no evidence was found for or against the effectiveness of common treatments for hordeolum. Controlled clinical trials would be useful in showing which treatments help people with acute internal hordeolum.

BACKGROUND

Description of the condition

Hordeolum is a common inflammation of the eyelid margin. It presents as a red, painful, swollen furuncle with an acute onset and is usually caused by a staphylococcal infection (Mueller 2008; Peralejo 2008; Skorin 2002). The infection can be internal, affecting the meibomian glands, or external, affecting the glands of Zeis or Moll (Wald 2004). External hordeola are known more commonly as styes. In many cases, the lesion drains spontaneously and resolves untreated; however, the infection can spread to other ocular glands or tissues, and recurrences are common. If unresolved, acute internal hordeolum can become chronic or can develop into a chalazion (De Jesus 2004; Hudson 1981; Mueller 2008; Rubin 1995).

Hordeolum is one of the most common diseases of the eye; therefore many people can be affected and many causative factors are known to be related to the disease. Incidence rates for hordeolum are not available because most cases are not reported. Hordeola tend to occur in younger people but are not limited to any age, gender, or racial group (Fuchs 1911; Lederman 1999; Roodyn 1954). Onset is spontaneous and may be related to lid hygiene, an

underlying condition, or a systemic infection (Mathew 1966; Wald 2004). Typically, the size of the swelling is a direct indicator of the severity of the infection (Lebensohn 1950). Internal hordeolum tends to be more painful and longer lasting than external hordeolum (Barza 1983; Fuchs 1911; Olson 1991; Wilkie 1956). Cases of recurrent hordeolum are usually the result of failure to eliminate bacteria completely rather than resulting from new infections (Roodyn 1954). Blepharitis (Fuchs 1911; Skorin 2002), acne rosacea (De Jesus 2004), trichiasis, and cicatricial ectropion (Moriarty 1982) are conditions frequently associated with internal hordeolum.

Most cases of internal hordeolum resolve on their own; therefore people with hordeolum often do not seek professional medical treatment (Olson 1991). Home therapies, including heated compresses, lid scrubs, and over-the-counter medications, are often employed without consultation with a medical professional. For times when medical care is sought, a general practitioner or a family physician may be consulted before an ophthalmologist or an optometrist is seen (Fraunfelder 1971; Lebensohn 1950).

Practice standards for the initial treatment of hordeola are conservative, typically limited to the application of warm compresses several times a day, if any treatment is recommended at all (Barza 1983; Fuchs 1911; Olson 1991; Panicharoen 2011; Sethuraman 2009; Wilkie 1956). A topical antibiotic may be prescribed in conjunction with warm compresses (Diegel 1986; Lebensohn 1950; Lederman 1999; Panicharoen 2011; Wald 2004). If the condition is severe and is resistant to topical antibiotics, systemic antibiotics or surgical incision and drainage may be implemented (Moriarty 1982; Mueller 2008; Panicharoen 2011; Rubin 1995; Skorin 2002).

Description of the intervention

Nonsurgical treatments for hordeolum include the application of warm or hot compresses, the use of lid scrubs and digital massage, the administration of antibiotics or steroids, or alternative medicine such as acupuncture and autohemotherapy. Typically, the intent of these interventions is to reduce healing time while relieving the symptoms associated with the lesion. Thus, interventions of interest would be provided during the first week after onset. Beyond one week, it is believed that internal hordeolum may resolve on its own or may require surgical incision and curettage. In addition to resolving the presenting hordeolum, other aims of the interventions are to minimize the risk that the infection may worsen, may spread to other areas, or may become recurrent.

How the intervention might work

The natural history of acute internal hordeolum generally spans one to two weeks, beginning with the appearance of an abscess and concluding with draining of the abscess. Initial treatments for hordeolum have therefore been aimed at promoting the evacuation of pus from the abscess. The application of a warm or hot compress may facilitate drainage by softening the granuloma (Diegel 1986; Fuchs 1911; Moriarty 1982; Skorin 2002). Heated compresses are typically employed for five to 10 minutes several times a day until the hordeolum is resolved.

Lid scrubs consist of mild shampoos or saline solutions and are applied while the affected area is gently massaged. The theory underlying the use of lid scrubs is that they promote lid hygiene and prepare the physical environment for drainage by clearing debris from the lid margin (Driver 1996; Skorin 2002). Creating a clear channel is believed to initiate drainage, similar to the epilation of an eyelash in cases of external hordeolum (Hudson 1981). Also, ingredients used in shampoos break down bacterial membranes, which further decreases the presence of bacteria at the infection site (McCulley 1984). Lid scrubs are commonly recommended in the treatment of other ocular bacterial infections, such as blepharitis, and may prevent the spread of infection (Avisar 1991). In conjunction with lid scrubs, lid massage has been proposed to physically express secretions from the infected glands (Driver 1996; Scobee 1942).

Antibiotics can be administered locally at the site of infection or may be given systemically. Most cases of hordeolum are caused by a staphylococcal species; therefore antibiotics should be effective against the bacteria. Application of topical antibiotics may reduce healing time by fighting against the causative bacterial infection and reducing inflammation. Many topical medications include ingredients that relieve the symptomatic pain of internal hordeolum. Antibiotics can also be applied locally by injection. Systemic antibiotics are sometimes used when local antibiotics are not effective, or when the infection is not localized.

Steroids can be applied topically as ointments or eyedrops. Internal hordeolum has a short course; therefore as little as one steroid treatment could be effective in reducing healing time and relieving symptoms associated with the inflammation (King 1986; Palva 1983).

Why it is important to do this review

Acute internal hordeolum is a common disease experienced by a wide population. Although the course of the disease is relatively short, instances of internal hordeolum are painful and bothersome. Furthermore, improper management of the underlying cause of the infection may lead to recurrent infections or to the development of other disease. Despite the common recommendation to employ heated compresses, their efficacy in treating hordeolum has not been systematically reviewed. If heated compresses are indeed sufficient in treating hordeolum, then more rigorous interventions, such as antibiotics or steroids, may not be warranted for initial treatment. Conversely, comparing the effectiveness and safety of all available interventions, to determine which may be most beneficial to the individual, is also important. A summary of the evidence should assist patients and professionals in determining preferred methods of treatment.

OBJECTIVES

The objective of this review was to investigate the effectiveness and, when possible, the safety of nonsurgical treatments for acute internal hordeolum compared with observation or placebo.

METHODS

Criteria for considering studies for this review

Types of studies—This review was limited to randomized and quasi-randomized clinical trials. Examples of quasi-randomized allocation include using participants' birth dates, medical record numbers, or order of enrollment to determine treatment groups.

Types of participants—We were interested in studies of participants with a diagnosis of acute internal hordeolum. Studies of participants with only external hordeolum (stye), chronic hordeolum, or chalazia were excluded.

Types of interventions—Nonsurgical interventions were the primary focus of this review. We included trials that compared the use of hot or warm compresses, lid scrubs, antibiotics, or steroids with observation, placebo, or another active intervention for the treatment of acute internal hordeolum. Complementary and alternative therapies, such as acupuncture and bloodletting, were outside the scope of this review.

Types of outcome measures

Primary outcomes: The primary outcome for this review was the proportion of participants with complete resolution of hordeolum seven days after diagnosis. The seven-day period for resolution was selected because most cases of hordeolum resolve on their own at between one and two weeks. We also analyzed the proportion of participants with complete resolution of hordeolum after 14 days as a secondary outcome, when these data were available.

Secondary outcomes

- The proportion of participants requiring surgical incision and drainage after the treatment period or seven days after diagnosis.
- The incidence of chalazion after the treatment period or seven days after diagnosis.
- The incidence of recurrence of hordeolum after six months and after one year. A recurrent case was considered as any hordeolum that occurred after one month from the resolution of the initial hordeolum and at any location on the same eyelid, or as defined by the included study.
- The incidence of a secondary hordeolum during or after the treatment period or seven days after diagnosis. A secondary hordeolum was defined as a hordeolum that occurred within one month of the initial hordeolum and at a different location than the initial hordeolum, or as defined by the included study.

Adverse outcomes: We planned to report all adverse effects related to the treatment of hordeolum that were reported in the primary studies. Specific adverse outcomes of interest included conjunctivitis; eye irritation; discoloration of the eyelid, conjunctiva, and lens; and corneal damage.

Economic data: We planned to report economic data.

Quality of life data: We planned to report quality of life data.

Search methods for identification of studies

Electronic searches—We searched the Cochrane Central Register of Controlled Trials (CENTRAL) 2012, Issue 7, part of *The Cochrane Library*. www.thecochranelibrary.com (accessed 26 July 2012), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE, (January 1950 to July 2012), EMBASE (January 1980 to July 2012), Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to July 2012), the *meta*Register of Controlled Trials (*m*RCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 26 July 2012. In 2012 we modified the search strategy to include broader terms related to hordeolum.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), LILACS (Appendix 4), *m*RCT (Appendix 5), ClinicalTrials.gov (Appendix 6) and the WHO International Clinical Trials Registry Platform (ICTRP) (Appendix 7).

Searching other resources—We reviewed the reference lists from potentially eligible studies to identify further studies. In addition we used the Science Citation Index to search for references that cited potentially eligible studies (last searched on 11 Oct 2012 with no relevant studies identified).

Data collection and analysis

Selection of studies—Two review authors independently assessed the titles and abstracts from the electronic literature searches and the manual search to identify possible trials of interest according to the 'Criteria for considering studies for this review'. We designated each reference identified from the searches as (a) relevant, (b) possibly relevant, or (c) not relevant for this review. We retrieved full text copies of the articles if an abstract was classified as (a) or (b). Each article was then independently assessed by two people and was classified as (1) include in review, (2) awaiting classification, or (3) exclude from review. We resolved discrepancies between authors by consensus.

Data extraction and management—As no studies were identified for inclusion in this review, no data extraction or assessment of risk of bias was performed. If, in the future, relevant studies become available, we will undertake the following methods for updating this review.

Two review authors will independently extract data using the data extraction forms created by the Cochrane Eyes and Vision Group. For each included study, we will extract data on study characteristics, interventions, outcomes, cost, quality of life, and other relevant information. One review author will enter the data into Review Manager (RevMan 2012)

and a second review author will verify the data entry. Discrepancies between review authors will be resolved by the third review author.

Assessment of risk of bias in included studies—Two review authors will independently assess the risk of bias of included studies based on the methods provided in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Sources of potential bias affecting the quality of a study will be divided into six domains that include:

- Selection bias: sequence generation and allocation concealment.
- Performance bias: masking (blinding) of participants and study personnel.
- Detection bias: masking (blinding) of outcome assessors.
- Attrition bias: incomplete outcome data and rates of missing data among treatment groups.
- Reporting bias: selective outcome reporting.
- Other sources of bias: funding source and other potential sources of bias.

For every study included in the review, we will assess each domain grouping to have (a) low risk of bias, (b) unclear or not reported risk of bias, or (c) high risk of bias. Discrepancies between review authors will be resolved by a third review author. For studies classified as unclear or not reported, we will contact the authors of the study for further information in an attempt to reclassify the quality of the study. If no informative response is received within 6 weeks, we will assess the study on the basis of available information.

Measures of treatment effect—The measures of treatment effect will depend on the types of data presented in the included studies and will be identified by the definitions given in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011).

Dichotomous data: The primary outcome of interest, the proportion of participants with complete resolution of hordeolum at seven days after diagnosis, will be analyzed as a dichotomous variable: resolved versus not resolved. Data on the proportion of participants requiring surgical incision and drainage after treatment, the proportion of participants developing a chalazion after treatment, the proportion of participants with recurrent hordeola, and the number of secondary hordeola will also be analyzed as dichotomous data. We will report dichotomous data as a summarized risk ratio with 95% confidence interval.

Continuous data: We will report continuous data as a weighted mean difference with its standard deviation. We anticipate that available economic and quality of life data will be analyzed as continuous data.

Ordinal data: We will summarize ordinal data qualitatively.

Counts and rate data: We will summarize counts and rate data in rate ratios when the event is rare, and as continuous outcome data when the event is more common. We will analyze adverse events data as counts and rates.

Unit of analysis issues: The unit of analysis for this review will be an eyelid of an individual participant.

Dealing with missing data: We will contact authors of included studies in an attempt to obtain missing data. We will set the response time at six weeks and will document any communications with study authors. If data cannot be retrieved, we will impute data from the reported data in the study. We will report loss to follow-up when available.

Assessment of heterogeneity: We will test for statistical heterogeneity using the I^2 statistic and will examine clinical heterogeneity using forest plots.

Assessment of reporting biases: We will use funnel plots to assess the possibility of reporting biases if more than ten studies are available.

Data synthesis: If limited heterogeneity is suggested (defined here as $I^2 < 50\%$), we will perform meta-analyses using the random-effects model unless there are three or fewer trials, in which case we will use the fixed-effect model. If heterogeneity is detected, we will combine trial results by relevant, less heterogeneous subgroups if sufficient data are available. Otherwise we will describe the results individually.

Subgroup analysis and investigation of heterogeneity: We will investigate heterogeneity by conducting subgroup analyses provided sufficient information is available. Subgroups of interest include sex, age, use of contact lenses, including soft lenses versus hard lenses, and the frequency of hordeolum occurrences, coinfections, and other comorbidities at baseline.

Sensitivity analysis: We will investigate the impact of studies with a high likelihood of bias, or with missing data, as well as the impact of unpublished studies, using sensitivity analyses.

RESULTS

Description of studies

See: Characteristics of excluded studies.

Results of the search—A total of 517 references were identified by the electronic searches as of 21 June 2010. After the titles and abstracts were screened, 19 references were classified as being potentially relevant. All of these 19 references, which reported 18 unique studies, were excluded. For the update of this review, we identified 427 additional references from electronic searches as of 26 July 2012. After the titles and abstracts were screened, six references were classified as being potentially relevant. All of these six references, which reported five unique studies, were excluded.

Excluded studies—Overall 23 studies were excluded in this review. The reasons for exclusion are described in the table 'Characteristics of excluded studies'.

Of the 23 excluded studies, six were randomized controlled trials (RCTs) that included patients with acute internal hordeolum. The first included pediatric participants with lid inflammation and was conducted to evaluate the safety of loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension (Zylet®) in the pediatric population (Comstock 2012). As safety was the primary focus of the trial, the study population comprised participants with varying ocular inflammatory conditions and data were not collected by study investigators for specific conditions. The second study compared the effectiveness of a combined antibiotic ophthalmic solution with placebo in participants with internal and external hordeolum after surgical incision and curettage (Hirunwiwatkul 2005). All participants had been newly diagnosed and untreated before undergoing incision and curettage. A total of 14 participants were randomly assigned to each group, and results for participants with internal and external hordeolum were not reported separately. The study authors concluded that no evidence suggested differences in pain score, mass size, or duration of cure between groups. The remaining four RCTs evaluated complementary and alternative therapies, such as acupuncture and bloodletting, which were not under the scope of this review (Chen 2000; Gao 2001; Takama 2006; Xu 2004).

Risk of bias in included studies

No studies were included in this review, thus no risk of bias assessment was done.

Effects of interventions

No studies were included in this review, thus no effects of interventions were reported.

DISCUSSION

Summary of main results

No trials were identified for inclusion in this review.

Overall completeness and applicability of evidence

Most of the references identified from the search for this review were related to external hordeola (styes) or chalazion. By and large, the few references specific to acute internal hordeolum either reported recommendations for treatment without cited evidence or were reports of interventional case series, case studies, or other types of observational study designs. The only clinical trials found that included participants with acute internal hordeolum were not eligible for the review because they included multiple conditions and did not stratify by specific diagnoses included participants who underwent surgical treatment as a criterion for study enrollment, or evaluated treatments that were not under the scope of review. Furthermore, the bulk of the literature was published more than 20 years ago.

Potential biases in the review process

The primary source of bias for this review was anticipated to be selection bias, specifically, the identification and inclusion of relevant studies. Before beginning the review process, we

expected that few trials had been published on hordeolum, that various authors used different terminologies when referring to different classifications of hordeola (i.e. hordeolum, stye, chalazia, etc.), and that relevant studies may be obtained from older publications. We therefore designed a broad search strategy for the electronic databases to facilitate identification of potentially relevant studies. We also manually searched the reference lists of potentially relevant studies to identify older studies that may not be included in electronic databases.

To minimize bias during the process of selecting studies for this review, two review authors screened the references from the electronic search and independently classified them for inclusion or exclusion. We included potentially relevant references that mentioned any type of hordeolum or external eye inflammation for assessment at the full text level. Inclusion and exclusion were determined by using the definition of the disease given in the full text article. Furthermore, one review author screening the studies had a clinical background (JN), and one had a methodological background (KL).

Agreements and disagreements with other studies or reviews

Although it is the most recommended therapy for hordeola, the application of warm compresses has not been shown to be effective in accelerating healing time or reducing symptoms associated with hordeolum in a controlled trial. Moreover, no evidence indicates that warm compresses alone would eliminate the infection. It is also unclear whether medical treatment or lid hygiene is effective in treating acute internal hordeolum.

AUTHORS' CONCLUSIONS

Implications for practice

Common interventions for the treatment of acute internal hordeolum include warm compresses applied at home, topical medications and lid scrubs available over-the-counter, antibiotics or steroids, lid massages, and others. At this time evidence regarding the effectiveness of these nonsurgical interventions for treating acute internal hordeolum is insufficient. Clinical practice decisions should be based on physician judgment, and available treatment options should be discussed with patients.

Implications for research

Generally, RCTs are considered the gold standard for comparing the efficacy of interventions. However, because of the relative mildness and short duration of the disease, study participants may be limited to more severe cases that are not representative of the general population; recruitment of participants at onset may be challenging. Even with these considerations, controlled clinical trials would be useful in determining which interventions are effective for the treatment of acute internal hordeolum.

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Internal sources

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External sources

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APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor Hordeolum explode all trees

#2 (Hordeol* or stye or styes)

#3 MeSH descriptor Eye explode all trees

#4 (sty)

#5 (#3 AND #4)

#6 MeSH descriptor Meibomian Glands explode all trees

#7 (Meibomian* adj3 (gland* or cyst* or infection* or inflammat*))

#8 (tarsal adj3 (gland* or cyst* or infection* or inflammat*))

#9 (palpebral adj3 (gland* or cyst* or infection* or inflammat*))

#10 (conjunctiv* adj3 (gland* or cyst*))

#11 (gland* adj5 (zeis* or Moll*))

#12 (lid* or eyelid* or “eye margin”) adj3 inflammat*

#13 (lid* or eyelid* or “eye margin”) adj3 infection*

#14 (#1 OR #2 OR #4 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13)

Appendix 2. MEDLINE (OvidSP) search strategy

1. Randomized Controlled Trial.pt.
2. Controlled Clinical Trial.pt.(randomized or randomised).ab,ti.
3. placebo.ab,ti.
4. drug therapy.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8

9. exp animals/not humans.sh.
10. 9 not 10
11. exp hordeolum/
12. (Hordeol* or stye or styes).tw.
13. sty.tw.
14. exp eyes/
15. 14 and 15
16. exp meibomian glands/
17. (Meibomian* adj3 (gland* or cyst* or inflammat* or infection*)).tw.
18. (tarsal adj3 (gland* or cyst* or inflammat* or infection*)).tw.
19. (palpebral adj3 (gland* or cyst* or inflammat* or infection*)).tw.
20. (conjunctiv* adj3 (gland* or cyst*)).tw.
21. (gland* adj5 (zeis* or Moll*)).tw.
22. ((lid* or eyelid* or eye margin) adj3 inflammat*).tw.
23. ((lid* or eyelid* or eye margin) adj3 infection*).tw.
24. 12 or 13 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
25. 11 and 25

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville et al (Glanville 2006).

Appendix 3. EMBASE.com search strategy

#1 'randomized controlled trial'/exp

#2 'randomization'/exp

#3 'double blind procedure'/exp

#4 'single blind procedure'/exp

#5 random*:ab,ti

#6 #1 OR #2 OR #3 OR #4 OR #5

#7 'animal'/exp OR 'animal experiment'/exp

#8 'human'/exp

#9 #7 AND #8

#10 #7 NOT #9

#11 #6 NOT #10

#12 ’clinical trial’/exp

#13 (clin* NEAR/3 trial*):ab,ti

#14 ((singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*)):ab,ti

#15 ’placebo’/exp

#16 placebo*:ab,ti

#17 random*:ab,ti

#18 ’experimental design’/exp

#19 ’crossover procedure’/exp

#20 ’control group’/exp

#21 ’latin square design’/exp

#22 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21

#23 #22 NOT #10

#24 #23 NOT #11

#25 ’comparative study’/exp

#26 ’evaluation’/exp

#27 ’prospective study’/exp

#28 control*:ab,ti OR prospectiv*:ab,ti OR volunteer*:ab,ti

#29 #25 OR #26 OR #27 OR #28

#30 #29 NOT #10

#31 #30 NOT (#11 OR #23)

#32 #11 OR #24 OR #31

#33 ’hordeolum’/exp

#34 hordeol*:ab,ti OR stye:ab,ti OR styes:ab,ti

#35 sty:ab,ti

#36 ’eye’/exp

#37 #35 AND #36

#38 ’meibomian gland’/exp

#39 (meibomian* NEAR/3 (gland* OR cyst* OR inflammat* OR infection*)):ab,ti

#40 (tarsal NEAR/3 (gland* OR cyst* OR inflammat* OR infection*)):ab,ti

#41 (palpebral NEAR/3 (gland* OR cyst* OR inflammat* OR infection*)):ab,ti

#42 (conjunctiv* NEAR/3 (gland* OR cyst*)):ab,ti

#43 (gland* NEAR/5 (zeis* OR moll*)):ab,ti

#44 ((lid* OR eyelid* OR 'eye margin') NEAR/3 inflammat*):ab,ti

#45 ((lid* OR eyelid* OR 'eye margin') NEAR/3 infection*):ab,ti

#46 #33 OR #34 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45

#47 #32 AND #46

Appendix 4. LILACS search strategy

Hordeol$ OR stye OR styes OR sty OR Meibomian$ OR (Tarsal gland$ OR tarsal cyst$ OR tarsal inflammat$ or tarsal infection$ OR palpebral gland$ OR palpebral cyst$ OR palpebral inflammat$ OR palpebral infection$) OR ((conjunctiv$) AND (gland$ OR cyst$)) OR ((zeis $ OR moll$) AND (gland$)) OR (Eyelid$ AND (inflammat$ OR infection$))

Appendix 5. metaRegister of Controlled Trials search strategy

Hordeolum OR hordeola OR stye OR styes OR sty OR Meibomian OR Eyelid inflammation

Appendix 6. ClinicalTrials. gov search strategy

Hordeolum OR hordeola OR stye OR styes OR sty OR Meibomian OR Eyelid inflammation OR Tarsal gland OR tarsal cyst OR tarsal inflammation or tarsal infection OR palpebral gland OR palpebral cyst OR palpebral inflammation OR palpebral infection OR conjunctiva gland OR conjunctiva cyst

Appendix 7. WHO International Clinical Trials Registry Platform search strategy

Hordeolum OR hordeola OR stye OR styes OR Meibomian OR Eyelid inflammation OR Tarsal gland$ OR tarsal cyst$ OR tarsal inflammation or tarsal infection$ OR palpebral gland$ OR palpebral cyst$ OR palpebral inflammation OR palpebral infection$ OR conjunctiva gland$ OR conjunctiva cyst$

DATA AND ANALYSES

This review has no analyses.

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* Indicates the major publication for the study

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Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bahgat 1986	Not population of interest: controlled trial of participants with chalazia, defined as chronic lipogranulomas with duration of one month to three years before therapy. Participants were stratified by type of chalazia and were assigned to injections of corticosteroids with or without antibiotics, or to control
Chen 2000	Not intervention of interest: RCT of participants with internal and external hordeolum randomly assigned to bloodletting of the ear or no treatment
Comstock 2012	Not population of interest: RCT of pediatric participants with lid inflammation to evaluate the safety and efficacy of Zylet® compared with vehicle. As the focus of the trial was primarily safety of Zylet® in pediatric patients, eligibility criteria were not strict and subgroup data for specific diagnoses were not collected
Copeman 1958	Not population of interest: controlled trial of participants with recurrent external hordeola, defined as at least one previous stye of the eyelash follicle within the last month. Patients alternately assigned to antibiotic ointment or control applied to the anterior nares
Gao 2001	Not intervention of interest: RCT of participants with hordeolum randomly assigned to wrist-ankle acupuncture or oral ofloxacin plus topical chloramphenicol
Garrett 1988	Not population of interest: RCT of participants with chalazia, defined as chronic inflammation of the meibomian glands. Participants randomly assigned to warm compresses and lid scrubs, intralesional steroid injections, or both treatments
Hatano 1969	Not population of interest: interventional case series of participants with ophthalmic infection. Of the 28 participants studied, 10 were diagnosed with hordeolum, but internal and external cases were not specified. All participants received topical minocycline
Hatano 1974	Not population of interest: interventional case series of participants with ophthalmic infection. Of the 40 participants studied, 10 were diagnosed with hordeolum, but internal and external cases were not specified. Four of these participants underwent surgery at the time of first consult, and six received the antibiotic amikacin
Hirunwiwatkul 2005	Not intervention of interest: RCT of participants with internal and external hordeolum after undergoing surgical incision and curettage. Participants randomly assigned to treatment with antibiotic ophthalmic solution or placebo after surgery
Jacobs 1984	Not population of interest: RCT of participants with noninfectious chalazia present for two or more weeks. Participants randomly assigned to injection with triamcinolone or incision and curettage
Kastl 1987	Not population of interest: RCT of participants with active eyelid infection (styes and blepharitis) determined by cultures taken from the base of the eyelashes. Participants randomly assigned to treatment with yellow mercuric oxide or placebo
Magnuson 1967	Not population of interest: interventional case series of participants with various eye infections, with most having conjunctivitis, meibomianitis, or blepharitis. Of the 131 participants studied, as many as three may have had stye. All participants received gentamicin sulfate and hot and cold compresses
Manabe 1981	Not population of interest: CCT of participants with infection of the anterior portion of the eye. Participants were assigned by order of enrollment to treatment with to bramycin ophthalmic solution or gentamicin ophthalmic solution. Of the 504 participants studied, 43 were diagnosed with hordeolum, but internal and external cases were not specified. Data were not reported separately for hordeolum cases
Mathew 1966	Not population of interest: interventional case series of participants with external hordeola, defined as acute inflammations of the glands situated at the root of eye lashes. All participants received penicillin and streptomycin plus a polyvalent antigen (Munomycin)
Oishi 1973	Not a controlled trial: interventional case series of 26 children with ophthalmic infection, 3 of whom had internal hordeolum. All participants received topical clindamycin-2-palmitate
Panda 1987	Not population of interest: controlled trial of participants with chalazia, defined as chronic inflammatory granulomas. Participants assigned to injection with one of three corticosteroids: dexamethasone, hydrocortisone, or triamcinolone
Sawae 1971	Not population of interest: interventional case series of participants with ophthalmic infection. Of the 22 participants studied, 1 was diagnosed with hordeolum, but it was not specified as being internal or external. All patients received clindamycin
Takama 2006	Not intervention of interest: RCT of participants with hordeolum randomly assigned to receive Chinese herbal medicine or no Chinese herbal medicine supplementary to topical ofloxacin and fluorometholone
Vácha 1987	Not population of interest: observational study of participants with chalazia, defined as granulomas. Treatment with kenalog injections was compared with incision and curettage
Wang 1983	Not population of interest: controlled trial of participants with chalazia, defined as tarsal cyst. Participants assigned to local injection of one of two corticosteroids

Study	Reason for exclusion
Watson 1984	Not population of interest: controlled trial of participants with chalazia, defined as chronic granulomas. Participants alternately assigned to injection with triamcinolone acetonide or incision and curettage
Willcox 2008	Not population of interest: case report of a participant treated with malian ointment for a stye
Xu 2004	Not intervention of interest: RCT of participants with hordeolum randomly assigned to acupuncture plus bloodletting of the ear or sham therapy

CCT: controlled clinical trial

RCT: randomized controlled trial