Assessing the Frequency of Spontaneous Clearance of Gonococcal Infection in the Absence of Antibiotic Therapy: a review of the literature

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Background

- In the last few decades, Neisseria gonorrhoeae has developed resistance against many different antimicrobials. Internationally there is increasing concern regarding the potential of “untreatable” gonorrhoea [1].
- Despite many countries employing dual antimicrobial therapy as first line treatment, cases with resistance to both ceftriaxone and azithromycin have been identified [2].
- Antimicrobial stewardship is essential for the control of antimicrobial resistance and includes the avoidance of antibiotics when not required.
- Clearance of gonorrhoea without treatment has been reported, yet there is little information regarding:
  - How often this occurs
  - The timescale within which it occurs
  - Whether it varies by site of infection
  - IF other factors, such as previous gonococcal infection, play a role
- We undertook a review of the literature:
  - To estimate the frequency of spontaneous clearance of gonococcal infection
  - To identify potentially important mediating factors
  - To inform priorities for future research

Methods

- Following initial scoping to establish terminologies, a literature search was performed using Medline, EMBASE, CINAHL, and Cochrane databases.
- Conference posters, oral presentations and letters to editor were included in addition to randomised controlled trials, non-randomised trials, cohort studies and case series.

The search identified 186 relevant papers – Figure 2
- 79 duplicates were removed and 98 papers excluded
- Conference posters, oral presentations and letters to editor were included in addition to randomised controlled trials, non-randomised trials, cohort studies and case series
- A variety of testing methods were used to detect N.gonorrhoeae; 6 studies used NAAT, 3 used culture and 1 used both.
- Populations included men and women with infection at a variety of anatomical sites
- Timescales between initial and repeat testing were variable (Figure 3)
  - 1 study demonstrated an increase in clearance rate at 14 days compared to 7 days after initial testing [3].
  - 2 studies performed sequential pharyngeal cultures; in 1 study all samples were negative by 7 days and in the other 55% of samples were negative by 7 days [4].
  - Overall spontaneous clearance rate was 9.7% (253/2618)

Results

- The search overall identified:
  - 10 cohort studies, with a total of 2618 patients
  - There was considerable heterogeneity between the studies and none was specifically designed to assess spontaneous infection clearance

Discussion

- Few available studies include information on how frequently spontaneous clearance of gonorrhoea occurs
- The majority of the studies reviewed were published as conference abstracts and lack methodological detail and in depth results on which to draw firm conclusions
- The reversion of an initially positive test result to negative (without treatment) could be due to:
  - ‘spontaneous’ clearance by the host immune system
  - An initial false positive test result
- Confirming spontaneous clearance is difficult because:
  - Testing methodologies vary in their sensitivity and specificity.
  - Culture is less sensitive than NAAT but 100% specific. NAAT has high sensitivity and specificity but its positive predictive value may still be low in low prevalence populations. False positive NAAT results may also arise from detection of commensal Neisseria species, especially at the pharynx.
- Using a combination of test approaches (e.g. culture and NAAT) will help to identify how frequently spontaneous clearance of infection occurs

- The majority of studies have evaluated pharyngeal clearance, there is little data on rectal, urethral, vulvovaginal and endocervical sites.
- There is insufficient evidence at present to accurately estimate how quickly spontaneous clearance might occur
- One study from 1979 [5] reported spontaneous clearance of pharyngeal gonorrhoea (using culture) in all patients by 12 weeks. Although this has not been replicated using the more sensitive NAAT, epidemiological evidence suggests that pharyngeal gonorrhoea persists for an average of 4 months and that untreated rectal gonorrhoea may persist for around 1 year [6].
- This current review identifies important gaps in our knowledge regarding spontaneous clearance of gonorrhoea, especially at sites other than the pharynx.
- The available literature suggests that 6-27% of those with gonorrhoea will clear their infection without treatment over a period of several weeks. This is a significant proportion and, if confirmed, suggests that use of a point of care test to confirm infection before treatment may be useful to avoid inappropriate antimicrobial use.

References