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Brand M, Grieve A

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TABLE OF CONTENTS

[Intervention Review]

Prophylactic antibiotics for penetrating abdominal trauma

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ABSTRACT

Background

Penetrating abdominal trauma occurs when the peritoneal cavity is breached. Routine laparotomy for penetrating abdominal injuries began in the 1800s, with antibiotics first being used in World War II to combat septic complications associated with these injuries. This practice was marked with a reduction in sepsis-related mortality and morbidity. Whether prophylactic antibiotics are required in the prevention of infective complications following penetrating abdominal trauma is controversial, however, as no randomised placebo controlled trials have been published to date. There has also been debate about the timing of antibiotic prophylaxis. In 1972 Fullen noted a 7% to 11% post-surgical infection rate with pre-operative antibiotics, a 33% to 57% infection rate with intra-operative antibiotic administration and 30% to 70% infection rate with only post-operative antibiotic administration. Current guidelines state there is sufficient class I evidence to support the use of a single pre-operative broad spectrum antibiotic dose, with aerobic and anaerobic cover, and continuation (up to 24 hours) only in the event of a hollow viscus perforation found at exploratory laparotomy.

Objectives

To assess the benefits and harms of prophylactic antibiotics administered for penetrating abdominal injuries for the reduction of the incidence of septic complications, such as septicaemia, intra-abdominal abscesses and wound infections.

Search methods

Searches were not restricted by date, language or publication status. We searched the following electronic databases: the Cochrane Injuries Group Specialised Register, CENTRAL (The Cochrane Library 2019, issue 7 of 12), MEDLINE (OvidSP), Embase (OvidSP), ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED), ISI Web of Science: Conference Proceedings Citation Index- Science (CPCI-S) and PubMed. Searches were last conducted on 23 July 2019.

Selection criteria

All randomised controlled trials of antibiotic prophylaxis in patients with penetrating abdominal trauma versus no antibiotics or placebo.

Data collection and analysis

Two authors screened the literature search results independently.

Main results

We identified no trials meeting the inclusion criteria.

Authors' conclusions

There is currently no information from randomised controlled trials to support or refute the use of antibiotics for patients with penetrating abdominal trauma.

PLAIN LANGUAGE SUMMARY

Should prophylactic antibiotics be used in patients with penetrating abdominal trauma?

For over half a century antibiotics have been given to patients that have suffered from a penetrating injury to the abdominal peritoneal cavity in an attempt to decrease the incidence of post-operative wound infection, intra-abdominal infection and mortality. This review was designed to assess whether or not this practice is supported by medical evidence.

No randomised controlled trials could be found that met the inclusion criteria for this review. Therefore, there is no evidence to unequivocally support or refute this practice. Current guidelines are based on expert opinion rather than fact.

We recommend that a randomised controlled trial be designed to assess which patients would benefit from antibiotic prophylaxis, and which patients would not. Hopefully this would result in less unnecessary antibiotic use, and thus less antibiotic resistance.

BACKGROUND

Penetrating abdominal trauma occurs when the peritoneal cavity is breached. Routine laparotomy for penetrating abdominal injuries began in the 1800s, but the discovery of penicillin in 1928 by Alexander Fleming allowed antibiotics to be used in the second World War to combat septic complications (Poole 1944). This practice was marked by a reduction in sepsis related mortality and morbidity. This was later ratified during the Korean war when casualties were given prophylactic antibiotics while awaiting transfer to hospital for further management (Scott 1954). Whether prophylactic antibiotics are required in the prevention of infective complications following penetrating abdominal trauma today is controversial as no randomised, placebo controlled trials have been published to date. Now, with the use of new sterilisation techniques for both surgical instruments and the surgical field, and a change in thinking with regard to hollow viscus perforation management, there may be a shift in the need for antibiotic usage in penetrating abdominal trauma.

There has also been debate about the timing of antibiotic prophylaxis. In 1972 Fullen noted a 7% to 11% post-surgical infection rate with pre-operative antibiotics, a 33% to 57% infection rate with intra-operative antibiotic administration and a 30% to 70% infection rate with only post-operative antibiotic administration (Fullen 1972). According to current guidelines there is sufficient class I evidence to support the use of a single pre-operative broad spectrum antibiotic dose with aerobic and anaerobic cover (Thadepalli 1972; Thadepalli 1973), with continuation (up to 24 hours) only in the event of a hollow viscus perforation found at exploratory laparotomy (Luchette 2000).

The aim of this review was to assess the benefits or harms of prophylactic antibiotics administered for penetrating abdominal injuries in terms of reducing the incidence of septic complications, such as septicaemia, intra-abdominal abscesses and wound infections.

OBJECTIVES

To assess whether there was a reduction in the incidence of infective complications following the administration of prophylactic antibiotics in penetrating abdominal trauma (wounds that enter the peritoneal cavity).

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials.

Types of participants

Patients who had an isolated penetrating abdominal wound, were not on antibiotics, and had no evidence of intra-abdominal sepsis or any other focus of infection.

Types of interventions

- Prophylactic antibiotic administration at the time of presentation to the emergency department, or perioperatively.
- Placebo or no antibiotic.

Trials would have been included regardless of the type, dose or route of administration of the antibiotic(s).

Types of outcome measures

Primary outcomes

- Septic complications, including intra-abdominal abscesses and wound infections.

Secondary outcomes

- Mortality.
- Septicaemia.

Search methods for identification of studies

Searches were not restricted by date, language or publication status.

Electronic searches

The Cochrane Injuries Group Information Specialist searched the following databases:

- Cochrane Central Register of Controlled Trials (CENTRAL; 2019, Issue 7) in the Cochrane Library (searched 23 July 2019);
- MEDLINE Ovid and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (1946 to 23 July 2019);
- Embase Classic + Embase Ovid (1947 to 23 July 2019);
- Clarivate Analytics Web of Science databases:
  * Science Citation Index Expanded (1970 to 23 July 2019);
  * Conference Proceedings Citation Index - Science (1990 to 23 July 2019);
  * Emerging Sources Citation Index (2015 to 23 July 2019).

The search strategy for the 2019 search can be found in Appendix 1, and the original search strategy used for the review versions published in 2009 and 2013 can be found in Appendix 2.

Searching other resources

We screened the reference lists of published articles for potential studies. We also searched the following clinical trials registries:

1. ClinicalTrials.gov (http://www.clinicaltrials.gov/; searched 23 July 2019);
2. Current Controlled Trials (http://www.controlled-trials.com/; searched 23 July 2019).

Data collection and analysis

Selection of studies

A total of 8610 references were retrieved by the search. For the 2019 update, two authors of Herrod 2019 independently screened the updated search. For the previous 2013 version of this review, MAB and ANG independently screened the search results to identify relevant trials.

None of the study reports found met the inclusion criteria. No trials were identified for inclusion in the review.

Data extraction and management

Had suitable studies been found, MAB and ANG would have independently extracted the following data from identified trials:

- year and language of publication;
- year of study;
- inclusion and exclusion criteria;
- sample size;
- mechanism of injury;
- type, dose and route of prophylactic antibiotic; and
- incidence of complications.

Assessment of risk of bias in included studies

MAB and ANG would have assessed the risk of bias of each trial independently. MAB and ANG would have recorded whether or not the trial authors performed their analysis using an intention-to-treat method. We would have clarified any unclear or missing information through contact with the trial report authors. We would have resolved differences in opinion between the review authors during extraction of data through discussion. JAG was to have served as arbitrator, should differences in opinion have persisted.

MAB and ANG would have assessed the risk of bias of the trials independently, without masking trial names. The review authors would have followed the instructions given in chapter 8 of *the Cochrane Handbook* (Handbook 2008). Due to the risk of biased overestimation of intervention effects in randomised trials that are of inadequate methodological quality (Kjaergard 2001; Moher 1998; Schulz 1995), the review authors would have looked at the influence of the methodological quality of the trials on the results by evaluating the reported randomisation and follow-up procedures in each trial. Where information was not available in the published trial reports, MAB and ANG would have contacted the authors in order to assess the trials correctly.

The review authors would have assessed generation of allocation sequence, allocation concealment, blinding and follow up. We would have presented this information in the 'Risk of bias' table in the review.

Allocation concealment

We would have judged allocation concealment as follows.

- Low risk of bias: if performed by means of centralised or pre-numbered containers administered serially to patients, or an on-site computer with allocations in a locked unreadable file, or sequentially-numbered, sealed, opaque envelopes.
- Unclear: if the trial is described as randomised, but the trial report fails to describe the method of allocation concealment.
- High risk of bias: if a completely transparent procedure was used, e.g. case record numbers, dates of birth, or an open list of random numbers.

Allocation sequence generation

We would have judged allocation sequence generation as follows.

- Low risk of bias: if a computer-generated or random-number table was used.
- Unclear: if the trial is described as randomised, but the trial report fails to describe the method of allocation sequence.
- High risk of bias: if patients were allocated according to names, dates, admittance numbers, etc. Trials using these methods are known as quasi-randomised trials, and would have been excluded from the review.

Blinding

We would have judged blinding as follows.

- Low risk of bias: if the trial was described as double blind, and the method of blinding was described.
- Unclear: if the trial was described as double blind, but the method of blinding was not described.
- High risk of bias: if the trial was not double blind.

Follow up

We would have judged follow up as follows.

- Low risk of bias: if the numbers and reasons for drop-outs and withdrawals in all intervention groups were described, or if it was specified that there were no drop-outs or withdrawals.
- Unclear: if the trial report gave the impression that there had been no drop-outs or withdrawals, but this was not specifically stated.
- High risk of bias: if the numbers or reasons for drop-outs and withdrawals were not described.

MAB and ANG would have recorded sample sizes and durations of follow up.

The authors would have used a funnel plot to explore bias (Macaskill 2001). We would have performed the linear regression approach described by Egger et al to determine funnel plot asymmetry (Egger 1997).

Measures of treatment effect

We would have analysed dichotomous data for risk ratio (RR) and odds ratio (OR), and measured the absolute effects with risk differences (RD). We would have calculated confidence intervals (CIs) at 95% for these measures of effect. We would also have considered treatment effect by intention-to-treat analysis, using available case analysis and analysis by imputation. We would have used the Mantel-Haenszel method for the meta-analysis (Greenland 1985; Mantel 1959). We would have presented results as a forest plot. We would have used the Cochrane Collaboration's Review Manager software for data analysis (Review Manager 2008).

Subgroup analysis and investigation of heterogeneity

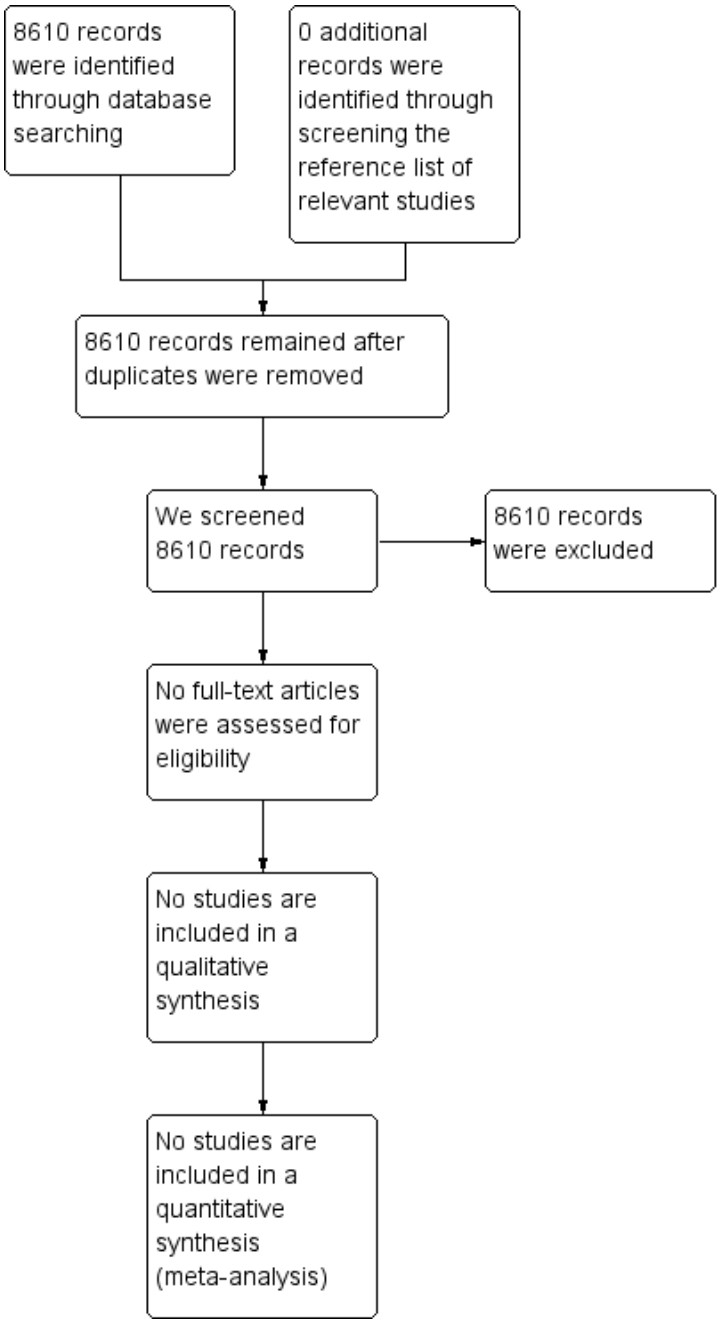
We would have tested statistical heterogeneity using the I^2 test (Higgins 2002) and the Chi^2 test, with a P value of 0.10 representing statistical significance. If heterogeneity was identified, we would have considered performing subgroup analyses. Subgroups that would then have been considered include: injury severity scores, time to surgical intervention, organs injured, different antibiotics and trials with a low risk of bias (adequate generation of allocation sequence, allocation concealment, blinding and follow up) compared to trials with a high risk of bias (one or more of the four components of methodological quality judged as being inadequate or unclear). If the results in the fixed-effect and random-effects models did not differ, we would have reported the fixed-effect model. Otherwise, we would have reported the results of both models.

RESULTS

Description of studies

The search resulted in 8610 potentially relevant references. There were no randomised controlled trials that fulfilled our inclusion criteria. The study selection process is summarized in the PRISMA flow diagram (Figure 1).

Figure 1. Study flow diagram.



Risk of bias in included studies

We could not identify any trials to include in this review.

Effects of interventions

We could not identify any trials to include in this review.

DISCUSSION

Since the discovery of penicillin in 1928 there has been a marked reduction in post-operative septic complications. This is especially true during war situations with prolonged extraction times, and delay to surgical intervention (Scott 1954). Antibiotics were introduced in the trauma setting almost 100 years ago (Poole

1944) with little thought as to their appropriate use. Improved surgical technique and equipment, together with surgical site preparation, post-operative care and the concept of expedient management has resulted in further improvement in mortality and morbidity figures.

We asked the question of whether or not we should be using prophylactic antibiotics with penetrating abdominal trauma. However we were not able to include any studies in this review, and thus cannot draw any conclusions about whether prophylactic antibiotics have an effect on septic complications, mortality or septicaemia compared to no antibiotic or a placebo.

This review has illustrated the fact that prophylactic antibiotic guidelines for penetrating abdominal trauma are based on expert opinion rather than firm evidence.

As prophylactic antibiotics are recommended by current guidance, another review has examined the evidence from head-to-head trials of different prophylactic antibiotics and duration of use for penetrating abdominal trauma (Herrod 2019).

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence from randomised controlled trials upon which to base the use of prophylactic antibiotics in patients with penetrating abdominal trauma (PET).

As prophylactic antibiotics are recommended by current guidance and currently in use for PET, another review has looked at the evidence from head-to-head trials regarding prophylactic antibiotic choice and duration of use for PET (Herrod 2019).

Implications for research

With the emergence of multiple-drug resistant organisms the use of antibiotics should be carefully considered. Placebo controlled, randomised, double blind studies are required to determine which patients, if any, would benefit from antibiotic prophylaxis in penetrating abdominal trauma.

ACKNOWLEDGEMENTS

We would like to thank Dr Jacque Goosen for his contribution to the protocol and first version of the review. We would also like to acknowledge the authors of Herrod 2019 for screening an updated search current to 23 July 2019 for their review looking at head-to-head trials of prophylactic antibiotics for penetrating abdominal trauma, which we used to inform our updated search.

We would like to thank the Cochrane Injuries Group for their editorial support.

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APPENDICES

Appendix 1. Search strategy for the 2019 version of the review

Cochrane Injuries Group Specialised Register

((((abdominal or abdomen or thorax or thoracic) AND (injur* or trauma* or perforat* or penetrat*))) OR (((splenic or spleen) AND (rupture*)) or ((stomach or gastric) AND (rupture or perforation or injur* or burst*)) or ((stab* or gunshot or shot or "penetrat* wound*") AND (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic))) AND (((antibiotic*) AND (prophylaxis or prophylactic* or premedication*)) or ((antibacterial or anti-bacterial) AND (agent*)))) AND (INREGISTER)

Cochrane Central Register of Controlled Trials (CENTRAL, in the Cochrane Library)

#1 MeSH descriptor: [Abdominal Injuries] explode all trees (140)

#2 MeSH descriptor: [Thoracic Injuries] explode all trees (382)

#3 ((abdominal or abdomen or thorax or thoracic) near/3 (injur* or trauma* or perforat* or penetrat*)):ti,ab,kw (936)

#4 ((splenic or spleen) near/3 rupture*):ti,ab,kw (16)

#5 ((stomach or gastric) near/3 (rupture or perforation or injur* or burst*)):ti,ab,kw (406)

#6 ((stab* or gunshot or shot or penetrat* wound* or bullet?) near/3 (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic)):ti,ab,kw (818)

#7 MeSH descriptor: [Wounds, Stab] explode all trees (106)

#8 MeSH descriptor: [Wounds, Gunshot] this term only (49)

#9 MeSH descriptor: [Wounds, Penetrating] this term only (170)

#10 MeSH descriptor: [Rupture] explode all trees (910)

#11 #7 or #8 or #9 or #10 (1219)

#12 (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic):ti,ab,kw (74440)

#13 #11 and #12 (175)

#14 #1 or #2 or #3 or #4 or #5 or #6 or #13 (2373)

#15 MeSH descriptor: [Antibiotic Prophylaxis] this term only (1224)

#16 (antibiotic* near/5 (prophylaxis or prophylactic* or premedication*)):ti,ab,kw (5052)

#17 MeSH descriptor: [Anti-Bacterial Agents] explode all trees (11257)

#18 ((antibacterial or anti-bacterial) near/3 agent*):ti,ab,kw (10428)

#19 MeSH descriptor: [Amoxicillin] explode all trees (2628)

#20 MeSH descriptor: [Ampicillin] this term only (990)

#21 (amox*):ti,ab,kw (5894)

#22 (clavulan*):ti,ab,kw (1775)

#23 MeSH descriptor: [Cefotaxime] explode all trees (1384)

#24 MeSH descriptor: [Cephalosporins] this term only (1381)

#25 (cefotaxim*):ti,ab,kw (1041)

#26 (ceftriaxone):ti,ab,kw (1571)

#27 MeSH descriptor: [Piperacillin] explode all trees (403)

#28 (piperac*):ti,ab,kw (957)

#29 (tazobactam):ti,ab,kw (620)

#30 MeSH descriptor: [Thienamycins] explode all trees (480)

#31 (meropenem):ti,ab,kw (608)

#32 (imipenem):ti,ab,kw (709)

#33 (cilastatin):ti,ab,kw (402)

#34 MeSH descriptor: [Ciprofloxacin] explode all trees (1139)

#35 (ciprofloxacin):ti,ab,kw (2635)

#36 MeSH descriptor: [Metronidazole] explode all trees (2161)

#37 (metronidazole):ti,ab,kw (4482)

#38 #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 (27206)

#39 #14 and #38 (170)

MEDLINE(R) Ovid, MEDLINE(R) Ovid In-Process & Other Non-Indexed Citations, MEDLINE(R) Daily Ovid, and OLDMEDLINE(R) Ovid

1. exp Abdominal Injuries/ (20049)

2. exp Thoracic Injuries/ (26101)

3. ((abdominal or abdomen or thorax or thoracic) adj3 (injur* or trauma* or perforat* or penetrat*)).ti,ab. (20348)

4. ((splenic or spleen) adj3 rupture*).ti,ab. (3700)

5. ((stomach or gastric) adj3 (rupture or perforation or injur* or burst*)).ti,ab. (5678)

6. ((stab* or gunshot or shot or penetrat* wound* or bullet?) adj3 (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic)).ti,ab. (1865)

7. exp Wounds, Stab/ (7770)

8. Wounds, Gunshot/ (14887)

9. Wounds, Penetrating/ (11421)

10. exp Rupture/ (46781)

11. or/7-10 (78662)

12. (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic).ti,ab. (687822)

13. 11 and 12 (16336)

14. or/1-6,13 [TOTAL ABDOMINAL INJURIES] (68171)

15. Antibiotic Prophylaxis/ (13160)

16. (antibiotic* adj5 (prophylaxis or prophylactic* or premedication*)).ti,ab. (16055)

17. exp Anti-Bacterial Agents/ (701868)

18. ((antibacterial or anti-bacterial) adj3 agent*).ti,ab. (8916)

19. exp Amoxicillin/ (10885)

20. Ampicillin/ (13297)

21. amox*.ti,ab. (17859)

22. clavulan*.ti,ab. (8078)

23. exp cefotaxime/ (11547)

24. cephalosporins/ (18937)

25. cefotaxim*.ti,ab. (8308)

26. ceftriaxone.ti,ab. (10054)

27. exp Piperacillin/ (2708)

28. piperac*.ti,ab. (7084)

29. tazobactam.ti,ab. (4391)

30. exp Thienamycins/ (6188)

31. meropenem.ti,ab. (5988)

32. imipenem.ti,ab. (9936)

33. cilastatin.ti,ab. (1307)

34. exp Ciprofloxacin/ (12859)

35. ciprofloxacin.ti,ab. (24424)

36. Metronidazole/ (12429)

37. metronidazole.ti,ab. (14893)

38. or/15-37 [ANTIBIOTICS] (736907)

39. randomi?ed.ab,ti. (578306)

40. randomized controlled trial.pt. (485792)

41. controlled clinical trial.pt. (93170)

42. placebo.ab. (199345)

43. exp Clinical Trials as Topic/ (328145)

44. randomly.ab. (314813)

45. trial.ti. (201916)

46. comparative study/ (1835236)

47. or/39-46 [CLINICAL TRIALS] (2931723)

48. animals/ not (humans/ and animals/) (4567683)

49. 47 not 48 (2434514)

50. 14 and 38 and 49 (150)

51. remove duplicates from 50 (149)

Embase Classic + Embase Ovid

1 exp abdominal injury/ (165983)

2 exp thorax injury/ (82196)

3 ((abdominal or abdomen or thorax or thoracic) adj3 (injur* or trauma* or perforat* or penetrat*)).ti,ab. (26160)

4 ((splenic or spleen) adj3 rupture*).ti,ab. (4797)

5 ((stomach or gastric) adj3 (rupture or perforation or injur* or burst*)).ti,ab. (7735)

6 ((stab* or gunshot or shot or penetrat* wound* or bullet?) adj3 (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic)).ti,ab. (2543)

7 stab wound/ (5413)

8 gunshot injury/ (19004)

9 penetrating trauma/ (12804)

10 exp rupture/ (114147)

11 or/7-10 (147285)

12 (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic).ti,ab. (1043589)

13 11 and 12 (24937)

14 or/1-6,13 [TOTAL ABDOMINAL INJURIES] (266153)

15 antibiotic prophylaxis/ (29984)

16 (antibiotic* adj5 (prophylaxis or prophylactic* or premedication*)).ti,ab. (23805)

17 exp antiinfective agent/ (3538995)

18 ((antibacterial or anti-bacterial) adj3 agent*).ti,ab. (12155)

19 amoxicillin/ (60295)

20 amoxicillin plus clavulanic acid/ (36320)

21 amoxicillin derivative/ (72)

22 ampicillin/ (86369)

23 ampicillin derivative/ (127)

24 amox*.ti,ab. (26820)

25 clavulan*.ti,ab. (11561)

26 cefotaxime/ (40281)

27 cephalosporin derivative/ (28049)

28 cefotaxim*.ti,ab. (11095)

29 ceftriaxone.ti,ab. (15527)

30 piperacillin/ (18896)

31 piperacillin plus tazobactam/ (24599)

32 piperacillin derivative/ (31)

33 piperac*.ti,ab. (11463)

34 tazobactam.ti,ab. (7730)

35 thienamycin derivative/ (447)

36 meropenem/ (29527)

37 meropenem.ti,ab. (10032)

38 imipenem/ (36081)

39 cilastatin plus imipenem/ (4655)

40 cilastatin/ (2644)

41 imipenem.ti,ab. (14420)

42 cilastatin.ti,ab. (1937)

43 ciprofloxacin/ (93985)

44 ciprofloxacin.ti,ab. (33573)

45 metronidazole/ (66235)

46 metronidazole.ti,ab. (21342)

47 or/15-46 [ANTIBIOTICS] (3553657)

48 exp controlled study/ (6968492)

49 comparative study/ (851033)

50 randomi?ed.ab,ti. (829337)

51 placebo.ab. (287657)

52 *Clinical Trial/ (19134)

53 major clinical study/ (3507971)

54 randomly.ab. (418211)

55 (trial or study).ti. (1936952)

56 or/48-55 [CLINICAL TRIALS] (10822904)

57 exp animal/ not (exp human/ and exp animal/) (5267381)

58 56 not 57 (8819418)

59 14 and 47 and 58 (8194)

ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) & Conference Proceedings Citation Index-Science (CPCI-S)

1 TOPIC: ((abdominal or abdomen or thorax or thoracic) near/3 (injur* or trauma* or perforat* or penetrat*)) (18,098)

2 TOPIC: ((splenic or spleen) near/3 rupture*) (2,350)

3 TOPIC: ((stomach or gastric) near/3 (rupture or perforation or injur* or burst*)) (5,711)

4 TOPIC: ((stab* or gunshot or shot or "penetrat* wound*" or bullet$) near/3 (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic)) (2,295)

5 #1 OR #2 OR #3 OR #4 (27,411)

6 TOPIC: (antibiotic* near/5 (prophylaxis or prophylactic* or premedication*)) (15,631)

7 TOPIC: ((antibacterial or anti-bacterial) near/3 agent*) (14,397)

8 TOPIC: (amox*) (19,583)

9 TOPIC: (clavulan*) (8,640)

10 TOPIC: (cefotaxim*) (7,653)

11 TOPIC: (ceftriaxone) (9,783)

12 TOPIC: (piperac*) (7,464)

13 TOPIC: (tazobactam) (4,669)

14 TOPIC: (meropenem) (6,082)

15 TOPIC: (imipenem) (9,687)

16 TOPIC: (cilastatin) (1,474)

17 TOPIC: (ciprofloxacin) (30,841)

18 TOPIC: (metronidazole) (16,452)

19 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 (114,359)

20 TOPIC: (randomi?ed OR randomly OR "random order" OR "random sequence" OR "random allocation" OR "randomly allocated" OR "at random" OR "randomi?ed controlled trial") (1.092,871)

21 TOPIC: ("controlled clinical trial" OR "controlled trial" OR "clinical trial" OR placebo) (592,530)

22 TOPIC: ((singl* OR doubl* OR trebl* OR tripl*) NEAR/5 (blind* OR mask*)) (269.973)

23 #20 OR #21 OR #22 (1,376,075)

24 #5 AND #19 AND #23 (68)

Appendix 2. Search strategy for the 2009 and 2013 versions of the review

Cochrane Injuries Group Specialised Register
(abdominal or abdomen or thorax or thoracic or splenic or spleen or stomach or gastric) and (injur* or trauma* or perforat* or penetrat* or rupture or burst* or stab* or gunshot or shot or wound*) and (Antibiotic or Prophylaxis or Gentamicin* or Cefazolin* or prophylactic* or premedication* or Cefazolin or cephazolin or cefamezine or cephamezine or ancef or cefamedin or gramaxin or kefzol or totacef or Tazobactam or piperacillin or tazocin or Gentamicin* or gentamycin* or gemyticin or gimyticin or gentacycol or gentavet or genticin or garamycin* or "co-amoxiclavulanic acid" or augmentin)

CENTRAL (*The Cochrane Library*)
#1 MeSH descriptor Abdominal Injuries explode all trees
#2 MeSH descriptor Thoracic Injuries explode all trees
#3 (abdominal or abdomen or thorax or thoracic) near3 (injur* or trauma* or perforat* or penetrat*)
#4 (splenic or spleen) near3 rupture*

#5 (stomach or gastric) near3 (rupture or perforation or injur* or burst*)
#6 (stab* or gunshot or shot or penetrat* wound*) near3 (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic)
#7 MeSH descriptor Wounds, Stab explode all trees
#8 MeSH descriptor Wounds, Gunshot explode all trees
#9 MeSH descriptor Rupture explode all trees
#10 abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic
#11 (#7 OR #8 OR #9)
#12 (#10 AND #11)
#13 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #12)
#14 MeSH descriptor Antibiotic Prophylaxis explode all trees
#15 MeSH descriptor Gentamicins explode all trees
#16 MeSH descriptor Cefazolin explode all trees
#17 (antibiotic*) near5 (prophylaxis or prophylactic* or remedication*)
#18 Cefazolin or cephazolin or cefamezine or cephamezine or ancef or cefamedin or gramaxin or kefzol or totacef or Tazobactam piperacillin or tazocin or Gentamicin* or gentamycin* or g-myticin or gmyticin or gentacycol or gentavet or genticin or garamycin* or co-amoxiclavulanic acid* or augmentin
#19 (#14 OR #15 OR #16 OR #17 OR #18)
#20 (#13 AND #19)

MEDLINE (OvidSP)
1.exp Abdominal Injuries/
2.exp Thoracic Injuries/
3.((abdominal or abdomen or thorax or thoracic) adj3 (injur* or trauma* or perforat* or penetrat*)).ab,ti.
4.((splenic or spleen) adj3 rupture*).ab,ti.
5.((stomach or gastric) adj3 (rupture or perforation or injur* or burst*)).ab,ti.
6.((stab* or gunshot or shot or penetrat* wound*) adj3 (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic)).ab,ti.
7.exp Wounds, Stab/
8.exp Wounds, Gunshot/
9.exp Rupture/
10.7 or 8 or 9
11.(abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic).ti,ab.
12.10 and 11
13.1 or 2 or 3 or 4 or 5 or 6 or 12
14.exp Antibiotic Prophylaxis/
15.exp Gentamicins/
16.exp Cefazolin/
17.(antibiotic* adj5 (prophylaxis or prophylactic* or premedication*)).ab,ti.
18.(Cefazolin or cephazolin or cefamezine or cephamezine or ancef or cefamedin or gramaxin or kefzol or totacef or Tazobactam piperacillin or tazocin or Gentamicin* or gentamycin* or g?myticin or gmyticin or gentacycol or gentavet or genticin or garamycin* or co?amoxiclavulanic acid* or augmentin).ab,ti.
19.14 or 15 or 16 or 17 or 18
20.13 and 19
21.(randomised or randomized or randomly or random order or random sequence or random allocation or randomly allocated or at random or controlled clinical trial$).tw,hw.
22.clinical trial.pt.
23.randomized controlled trial.pt.
24.randomized controlled trial.pt.
25.controlled clinical trial.pt.
26.placebo.ab.
27.clinical trials as topic.sh.
28.trial.ti.
29.21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
30.humans.sh.
31.29 and 30
32.20 and 31

Embase (OvidSP)
1.exp Abdominal Injury/
2.exp bite wound/ or exp gunshot injury/ or exp knife cut/ or exp missile wound/ or exp stab wound/
3.(abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic).ti,ab.
4.2 and 3

5.exp spleen rupture/ or exp aorta rupture/ or exp liver rupture/ or exp stomach rupture/ or exp thorax organ rupture/ or exp urogenital tract rupture/ or exp diaphragm injury/ or exp thorax penetrating trauma/
6.1 or 4 or 5
7.((abdominal or abdomen or thorax or thoracic) adj3 (injur* or trauma* or perforat* or penetrat*)).ab,ti.
8.((splenic or spleen) adj3 rupture*).ab,ti.
9.((stomach or gastric) adj3 (rupture or perforation or injur* or burst*)).ab,ti.
10.((stab* or gunshot or shot or penetrat* wound*) adj3 (abdomen* or abdominal or stomach or splenic or spleen or thorax or thoracic)).ab,ti.
11.6 or 7 or 8 or 9 or 10
12.exp Antibiotic Prophylaxis/
13.exp Gentamicin/
14.exp Cefazolin/
15.(antibiotic* adj5 (prophylaxis or prophylactic* or premedication*)).ab,ti.
16.(Cefazolin or cephazolin or cefamezine or cephamezine or ancef or cefamedin or gramaxin or kefzol or totacef or Tazobactam piperacillin or tazocin or Gentamicin* or gentamycin* or g?myticin or gmyticin or gentacycol or gentavet or genticin or garamycin* or co? amoxiclavulanic acid* or augmentin).ab,ti.
17.12 or 13 or 14 or 15 or 16
18.11 and 17
19.exp animal model/
20.Animal Experiment/
21.exp ANIMAL/
22.exp Experimental Animal/
23.19 or 20 or 21 or 22
24.Human/
25.23 not 24
26.(randomised or randomized or randomly or random order or random sequence or random allocation or randomly allocated or at random or controlled clinical trial* or placebo).tw,hw.
27.exp clinical trial/
28.exp Randomized Controlled Trial/
29.26 or 27 or 28
30.29 not 25
31.18 and 30

ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED)
ISI Web of Science: Conference Proceedings Citation Index-Science (CPCI-S)
1.Topic=(abdominal or abdomen or thorax or thoracic or splenic or spleen or stomach or gastric)
2.Topic=(injur* or trauma* or perforat* or penetrat* or rupture or burst* or stab* or gunshot or shot or penetrat* wound*)
3.Topic=(Antibiotic or Prophylaxis or Gentamicin* or Cefazolin* or prophylactic* or premedication* or Cefazolin or cephazolin or cefamezine or cephamezine or ancef or cefamedin or gramaxin or kefzol or totacef or Tazobactam piperacillin or tazocin or Gentamicin* or gentamycin* or gemyticin or gimyticin or gentacycol or gentavet or genticin or garamycin* or co-amoxiclavulanic acid* or augmentin)
4.Topic=(randomised or randomized or randomly or random order or random sequence or random allocation or randomly allocated or at random or placebo) OR Title=(trial or controlled)
5.1 and 2 and 3 and 4

PubMed
(((placebo[Title/Abstract]) OR drug therapy[MeSH Subheading] OR randomly[Title/Abstract] OR trials[Title/Abstract] OR group[Title/Abstract] OR randomized[Title/Abstract] OR randomised[Title/Abstract] OR controlled clinical trial[Publication Type] OR randomized controlled trial[Publication Type] NOT ((animals[MeSH Terms]) NOT humans[MeSH Terms]))) AND ((abdominal OR abdomen OR thorax OR thoracic OR splenic OR spleen OR stomach OR gastric) AND (injur* OR trauma OR traumatic OR perforat* OR penetrat* OR rupture OR burst* OR stab OR stabbed OR stabbing* OR gunshot OR shot OR wound*) AND (Antibiotic OR Prophylaxis OR Gentamicin* OR Cefazolin* OR prophylactic* OR premedication* OR Cefazolin OR cephazolin OR cefamezine OR cephamezine OR ancef OR cefamedin OR gramaxin OR kefzol OR totacef OR Tazobactam OR piperacillin OR tazocin OR Gentamicin* OR gentamycin* OR gentacycol OR gentavet OR genticin OR garamycin* OR augmentin))

WHAT'S NEW

Date	Event	Description
5 December 2019	New citation required but conclusions have not changed	The search has been updated to 23 July 2019. No new studies were identified and the conclusions remain the same.

Date	Event	Description
5 December 2019	New search has been performed	The review has been updated with a search to 23 July 2019. No studies are included in the review and the conclusions remain the same.

HISTORY

Protocol first published: Issue 4, 2008
Review first published: Issue 4, 2009

Date	Event	Description
23 July 2013	New search has been performed	The search has been updated to 16 January 2013.
23 July 2013	New citation required but conclusions have not changed	The search has been updated to 16 January 2013. No new studies were identified; the conclusions remain the same. The authors have changed.

CONTRIBUTIONS OF AUTHORS

Original version of the review (2009): MAB and ANG independently collected the referenced studies. MAB and ANG analysed studies for inclusion independently. MAB and ANG met to discuss the results. MAB wrote the initial manuscript, which was ratified by ANG and JAG. JAG supervised the review process.

2013 update: MAB and ANG screened the search results and made minor edits to the manuscript. Both authors agreed on the final version of the updated review.

DECLARATIONS OF INTEREST

MAB: None known

ANG: None known

INDEX TERMS

Medical Subject Headings (MeSH)

*Antibiotic Prophylaxis; Abdominal Injuries [*complications]; Anti-Bacterial Agents [therapeutic use]; Randomized Controlled Trials as Topic; Sepsis; Surgical Wound Infection [prevention & control]; Wound Infection [*prevention & control]; Wounds, Penetrating [*complications]

MeSH check words

Humans