Diagram D2: Meta-analysis of randomized trials using piperacillin-containing regimens exploring renal failure

Identification

Potentially relevant Randomized trials investigating piperacillin regimens:
PubMed search term [piperacillin]. Limits: “Randomized controlled trial”, “English” and “All adult: 19+ years”
(N=212)

Screening

Screened (N=212)

Excluded (N=78)
- Not RCT (unsystematic review, letter, comment): 9
- Economic study: 3
- Laboratory or other non-clinical study: 30
- Prophylaxis study (1-3 administrations): 33
- Not access to article (journal no longer exists or other reason): 3

Assessed for eligibility (N=134)

Excluded (N=127)
- Not investigating a piperacillin regimen: 31
- Piperacillin administered in both arms: 20
- All patients had end stage renal failure at baseline: 2
- N<50: 10
- Aminoglycoside in one or both arms: 39
- Did not report renal failure*: 25

Included

Included (N=7)

Renal failure defined biochemically or referred to any adopted standard: 2 (1, 2)
Renal failure not defined biochemically or referred to any adopted standard: 5 (3-7)

Results:

- In the initial identification phase, four ICU studies were found: They were excluded, since A) only a (non-defined) part of the patients received piperacillin(8), B) Both groups received piperacillin(9), C) one or both groups received aminoglycosides concomitantly(10, 11) .
- In the 7 (non-ICU) trials eventually included, 1592 episodes of therapy were observed.
- 21 cases of renal failure (not defined) occurred, corresponding to 1.3%.
- Hypothesizing, that the incidence of renal failure is 0.5% in non-piperacillin containing beta-lactam therapies, and aiming to find a risk increase to totally 1.5% (relative risk of 3.0), using conventional type I risk limit of 5% and a power of 80%, the sample size for such a trial investigating this should be approx. 3300 patients (non-ICU setting).
- In an ICU setting, the incidence of renal failure is often >20%. A trial of 1000 patients would be able to detect a risk increase to 28% (Relative risk:1.4) from e.g. piperacillin

*All articles were reviewed for this. Additionally, in adobe documents with the search option (those not scanned), a search was made in each pdf document with search terms: “renal”, “kidney”, “nephro”, “creatinine” and “gfr”. More than the noted 25 of the articles did not report renal failure, however, if they fulfilled one or more of the other exclusion criteria, they were excluded because of this.
References (for meta-analysis)


