Antibiotic therapy in hospital, oral versus intravenous treatment

This is an excerpt from the full technical report, which is written in Norwegian.

The excerpt provides the report's main messages in English.

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Norwegian Knowledge Centre for the Health Services summarizes and disseminates evidence concerning the effect of treatments, methods, and interventions in health services, in addition to monitoring health service quality. Our goal is to support good decision making in order to provide patients in Norway with the best possible care. The Centre is organized under The Norwegian Directorate for Health, but is scientifically and professionally independent. The Centre has no authority to develop health policy or responsibility to implement policies.

We would like to thank all contributers for their expertise in this project. Norwegian Knowledge Centre for the Health Services assumes final responsibility for the content of this report.

Norwegian Knowledge Centre for the Health Services
Oslo, 2010

Key messages

Antibiotic therapy in hospital, oral versus intravenous treatment

Background: This report addresses the following question: Is there a difference in efficacy between oral and intravenous antibiotic treatment of infectious diseases for large and important groups of patients. The report does not answer the question of when (how soon) you can change from intravenous to oral treatment.

Methods: We based this systematic review of a search for other systematic reviews in relevant bibliographic databases. For pneumonia and urinary tract infections, we also searched for randomized controlled trials. We compiled, analysed and graded the quality of the documentation. We summarized the results for six main outcomes: Total mortality, cure rates, treatment failure, re-admissions, length of stay in hospital and serious side effects.

Results: We included six systematic reviews which evaluated the effect of oral versus intravenous administration of antibiotics for pneumonia, urinary tract infection, osteomyelitis, spontaneous bacterial peritonitis, and febrile neutropenia in cancer patients. In addition, we included 10 randomized controlled trials. On the whole, we did not find significant differences between oral and intravenous administration of antibiotics. The quality of this documentation is low and the estimates are therefore uncertain.

Conclusion: The documentation provides no basis for determining whether there is difference in efficacy and side effects of oral versus intravenous administration of antibiotics. This does not mean that there are no differences in the administration route, but the results are too uncertain for us to draw conclusions about this.

Executive summary

Antibiotic therapy in hospital, oral versus intravenous treatment

BACKGROUND

Antibiotics are used to treat infectious diseases by killing or inhibiting the growth of microorganisms. Antibiotics may be administered orally, intravenously or intramuscularly. In some patients the absorption of antibiotics from the gastrointestinal system and thus the effect of oral administration can be unpredictable and antibiotics may be given intravenously. Intravenous administration can cause complications and will also put greater demands on staff resources.

To address the efficacy and safety for the different routes of administration, we have focused on infectious diseases that are common in hospitals and affect many patients. These are primarily community acquired pneumonia and urinary tract infections. We have tried to answer the following question:

Is there a difference in efficacy between oral versus intravenous antibiotic treatment of infectious diseases in large and important groups of patients?

The report does not answer the question of when (how soon) you can change from intravenous to oral treatment.

METHODS

The work with this systematic review was coordinated as a project where the Norwegian Knowledge Centre for the Health Services and specialists in infectious medicine participated. We searched for systematic reviews in relevant bibliographic databases in May 2008 and updated the search in November 2009. For pneumonia and urinary tract infections, we also searched for randomized controlled trials in August 2008. Two people went through all the titles and abstracts and selected the articles independently. We ordered relevant systematic reviews and primary articles in full text, assessed the quality using checklists and graded the overall documentation.

We summarized the results for efficacy and safety of six primary outcomes: Total mortality, cure rates, treatment failure, re-admissions, length of stay in hospital and serious side effects

For each intervention, we conducted separate meta-analysis for each of the comparisons with respect to the administration route. We have looked at the following comparisons:

- Oral (PO) versus intravenous (IV)
- PO versus IV with switch to PO
- IV versus IV with switch to PO

For pneumonia and urinary tract infection, we analyzed the results for children and adults separately. For pneumonia we also split the analysis into non-serious and serious pneumonia.

RESULTS

The literature search for systematic reviews identified 1646 references. We included six systematic reviews that assessed the effect of oral versus intravenous administration of antibiotics for pneumonia, urinary tract infection, osteomyelitis, spontaneous bacterial peritonitis, and febrile neutropenia in cancer patients.

The literature search for primary studies identified 1572 references. We included 10 randomized controlled trials that were not already included in the systematic reviews.

For all the outcomes and comparisons the quality of documentation is low and the estimates are therefore uncertain.

This means that even if the results show that we may have little or no difference (no statistically significant differences) between oral and intravenous treatment, this does not mean that there are no differenceses. The results are too uncertain for us to draw conclusions about this

Pneumonia

For children with severe pneumonia oral administration may lead to slightly fewer serious side effects than intravenous, OR 0.35 (95 % CI 0.16 til 0.80). For children with pneumonia (studies have included individuals with both non-severe and severe pneumonia), the results show little or no difference between oral and intravenous antibiotic treatment for almost all of the outcomes. We lack evidence for compari-

sons oral versus intravenous -> oral for children with non-severe pneumonia and intravenous versus intravenous -> oral for all groups.

For adults with pneumonia, the results also show little or no difference between oral and intravenous antibiotic treatment for almost all of the outcomes. For adults with non-severe pneumonia, oral administration may lead to slightly fewer serious side effects than intravenous, OR 0.45 (95 % CI 0.24 til 0.83). For adults with severe pneumonia, intravenous -> oral administration may lead to slightly fewer side effects than intravenous treatment, OR 2.90 (95 % CI 1.38 til 6.10). We lack evidence for comparisons oral versus intravenous for adults with severe pneumonia, and for adults with non-severe and severe pneumonia (studies have included individuals with both non-severe and severe pneumonia), for oral versus oral -> intravenous for adults with severe pneumonia and for intravenous versus intravenous -> oral for adults with non-severe pneumonia.

Urinary tract infections

For children with urinary tract infections, the results show little or no difference between oral and intravenous antibiotic treatment for almost all of the outcomes. The only significant difference is that intravenous -> oral may lead to slightly fewer adverse events than oral treatment, OR 5.57 (95 % CI 1.59 til 19.48).

For adults with urinary tract infection, the results also shows little or no difference between oral and intravenous antibiotic treatment for almost all of the outcomes, except that intravenous-> oral administration may lead to slightly shorter length of stay than intravenous administration, mean length of stay was 6.3 days longer for those who got intravenous treatment, (from 0.82 to 11.78 days longer).

Other infectious diseases

For spontaneous bacterial peritonitis, osteomyelitis, and febrile neutropenia in cancer patients, the quality of available research for most of the outcomes and comparisons is too low to determine whether there is any difference in effect between the administration routes, or we lack documentations for the outcomes. For some outcomes, the administration route may make little or no difference.

For the end point where we found results, it is perhaps little or no difference between the administration routes. This does not apply to intravenous treatment of febrile neutropenia in cancer patients that probably leads to fewer side effects which required end of treatment than oral administration, RR 5.76 (95 % CI 1.68 to 19.73) and fewer gastrointestinal side effects RR 5.14 (95 % CI 3.15 to 8.38).

DISCUSSION

We have summarized and assessed the overall documentation of the efficacy of oral versus intravenous antibiotic treatment of infectious diseases in hospitals. We have found evidence that fulfilled our inclusion criteria for pneumonia, urinary tract infection, osteomyelitis, spontaneous bacterial peritonitis, and febrile neutropenia in cancer patients.

The quality of the documentation is generally low or very low. This means that we are uncertain what the true effect of the intervention really is. This does not mean that we can conclude that the intervention does not work or that there is no difference between the two interventions. Overall, the studies included in this report were too small or too poorly designed to convince us as to whether a difference in effect is, or is not, present. New research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

We have considered if the results of the included studies can be transferred to a Norwegian setting. Different resistance situations in Norway and in the study countries will affect the assessment of the transferability. In a large proportion of the studies, at least one of the medicines that are used is not registered in Norway and thus not in common use. In addition, there are different traditions in different countries when it comes to which patients that are admitted to hospital, and also for whom one uses intravenous antibiotics. In some studies, it is used intramuscular administration, which is used in very limited extent in Norway. In relation to other countries, Norway has registered very few broad-spectre oral antibiotics. These are factors that may be important to be aware of when transferring the results to a Norwegian setting.

CONCLUSION

The documentation provides no basis for determining whether there is difference in efficacy and side effects of oral versus intravenous administration of antibiotics. This does not mean that there are no differences in the administration route, but the results are too uncertain for us to draw conclusions about this.

The report reveals the lack of high quality documentation when it comes to oral versus intravenous antibiotic use. We need more and better research for the large patient groups. Since the use of antibiotics and resistance conditions in Norway still differ somewhat from countries outside the Nordic region, there is a need for studies that are carried out in Norway or Scandinavia.

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