Reduction of the door-to-needle time for administration of antibiotics in patients with a severe infection: a tailored intervention project

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ABSTRACT

Background: Door-to-needle time (DNT), defined as the time between arrival at the emergency department (ED) and intravenous (iv) antibiotic administration is of crucial importance in the treatment of patients suffering from serious infections. The aim of this project was to reduce the DNT for patients with a serious infection as primary outcome parameter.

Methods: All adult patients arriving at the ED with a suspected infection for whom admission and iv antibiotics were indicated were included.

Results: Firstly, baseline DNT was measured and potential delaying factors were identified. Subsequently, five tailored interventions were implemented at regular intervals and their effects on the DNT were analysed. The interventions were: 1) additional resident attendance during peak hours, 2) immediate examination by residents prior to laboratory results, 3) chest X-ray at the ED instead of the external radiology department, 4) iv antibiotic administration at the ED instead of the ward and finally, 5) primary dipstick urine analysis at the ED.

A total of 295 patients were included (53.9% men), median age was 59 years (IQR 46 to 73). Median baseline DNT was 183 min (IQR 122 to 296). Implementation of the first three interventions did not reduce the DNT; however, after implementation of the fourth (administer all antibiotics at the ED) and finally all five interventions the DNT was reduced by 15.3% (p=0.040) to a final median DNT of 155 min (IQR 95 to 221).

Conclusion: Identification of delaying factors and implementation of tailored interventions reduces the DNT.

KEYWORDS

Door-to-needle time, hospital stay, infection, antibiotics

INTRODUCTION

A suspected severe infection is the main reason for admission to the Department of Internal Medicine in our hospital in nearly 40% of the patients. Almost all of these patients are admitted through the emergency department (ED). The optimal treatment of a patient with a severe infection encompasses many aspects. Besides proper supportive treatment and empirical therapy, the time between the arrival of the patient and administration of antimicrobial agents is a very important variable and correlates with better outcome. This so-called ‘door-to-needle time’ (DNT), defined as the time between arrival at the ED and administration of intravenous (iv) antibiotics, has been widely studied considering outcomes such as morbidity and mortality. The majority of studies focus on patients treated for the most common infection, i.e. pneumonia.

Retrospective studies showed positive associations between antibiotic administration within four to eight hours and a decreased mortality and an almost half day shorter length of stay in the hospital compared with a longer DNT. For example, in patients with meningitis (n=119) a similar association has been described between the effect of reduction of DNT and mortality. The study a DNT over six hours was associated with an 8.4 times greater risk of mortality. Hood et al. (1998) retrospectively studied patients with a urinary tract infection. They also concluded...
that timely (within four hours) antibiotic administration was associated with a shorter length of hospital stay.\textsuperscript{7} Based on these studies we presumed that DNT is an important denominator for treatment outcome and therefore should be a standard component of quality of care for patients with a severe infection. However, a reduction in the DNT has not yet been prospectively studied in a large population who presented to the ED with different kinds of infections. In this article, we describe the results of a health care improvement project, in which we tried to reduce the DNT (primary outcome) for all patients with a serious infection arriving at the ED of our hospital. Furthermore, we measured the result of these interventions on the duration of hospital stay (HS) and whether a shorter DNT was associated with presentation during office-hours (secondary outcome parameters).

\textbf{METHODOLOGY}

\textbf{Project group and interventions}

A prospective survey of medical records and prescription charts was performed at the Department of Internal Medicine of a tertiary teaching hospital in the Netherlands. Between March 2006 and December 2006 all adults presenting to the ED with a suspected infection, according to the ED physician and the attending internist, for whom admission and iv antibiotics were indicated, were considered to have a severe infection and included in the survey. No exclusion criteria were present, all patients were included. Several patient characteristics concerning vital signs, concomitant diseases, medication use, laboratory results (at least white blood counts and creatinine level) and readmissions within 30 days were noted on case record forms.

An expert group of all participating professionals: the project coordinator (C.T.), two ED nurses, two ED residents (M.V., S.W.), one logistic expert (R.R.), the head of the ED (J.L.), and the project leader (S.G.) analysed the results every month. Possible slowing factors and appropriate interventions to decrease the DNT were discussed. All interventions were sequentially introduced on the first day of the next month. Continuous measurements were obtained during this period.

\textbf{Implementation}

Interventions were strategically implemented by the contingency model.\textsuperscript{8} A questionnaire about the characteristics of the ED and the innovation (reducing the DNT) was sent to all residents of the Department of Internal Medicine and ED nurses. Firstly, we presented the results of the questionnaires, because we wanted the staff members to be aware of their basic assumptions. Hidden and unconscious opinions about this innovation among staff members could be brought out into the open by discussing the results of these questionnaires. Secondly, presentations were given at the beginning, half way through and at the end of the project. The aim of these presentations was to support and to start a decentralised management of the project. Thirdly, by stressing innovations or a particular result, we stimulated a ‘we-feeling’, which represents and promotes a team-oriented configuration.

\textbf{Statistics}

This project was a health innovation project rather than a conventional study. Therefore, we did not perform a sample size calculation, but included all consecutive patients with the suspicion of a severe infection during a pre-specified period. Distribution of the DNT and HS was expressed as median with corresponding inter-quartile range (IQR) unless stated otherwise. Differences in DNT and HS between intervention groups were tested with the Mann-Whitney U test. Differences in categorical data between groups were tested with the \( \chi^2 \) test. P values \( \leq 0.05 \) were considered statistically significant. Statistical analysis was performed by using SPSS 12.0.2 (SPSS Inc, Chicago, IL).

\textbf{RESULTS}

\textbf{Baseline characteristics}

Patient characteristics are summarised in table 1. A total of 295 patients were included (46.1\% female). Median age was 59.0 years (inter quartile range (IQR) 46 to 73). Diagnoses were reported when patients were dismissed from hospital. Consequently, 13.4\% of the patients suspected of having an infection in the ED did not have a discharge diagnosis of infection. During the project period, DNT and HS were measured in 60 patients before

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<thead>
<tr>
<th>Table I. Baseline characteristics</th>
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<tr>
<td>Characteristics</td>
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<td>N</td>
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<tr>
<td>Female (%)</td>
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<tr>
<td>Age\textsuperscript{a}</td>
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<tr>
<td>Infection diagnoses (%)</td>
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<tr>
<td>Respiratory tract infection</td>
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<td>Urinary tract infection</td>
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<td>Liver and biliary tract infection</td>
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<td>Skin/soft tissue infection</td>
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<td>Septicaemia</td>
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<tr>
<td>Intravenous catheter infection</td>
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<td>Fever of unknown focus</td>
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<tr>
<td>Neutropenic fever</td>
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<tr>
<td>Bone and joint infection</td>
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<tr>
<td>Other infections</td>
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<tr>
<td>None</td>
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\textsuperscript{a}Median (IQR)

Age is given in median with inter quartile range (IQR). All other numbers are percentages (%) of the total number of patients. None means that at the moment of discharge from the hospital it was clear that the patient did not have an infection, but had an alternative diagnosis.
implementation of the intervention, and in 22, 25, 47, 102 and 39 patients, respectively, after implementation of each of the five subsequent interventions. Different variables were studied (age, the percentage of patients who had concomitant chronic diseases such as diabetes, admission to the intensive care unit, positive blood cultures or death). No differences between the groups were noted.

**INTERVENTIONS AND DNT**

Baseline DNT was measured and potential delaying factors were identified. Sixty patients were included in this period. *Figure 1* shows the effects of implemented interventions on DNT during the project period. Median DNT at baseline was 183 minutes (IQR 122 to 296).

1. The first intervention consisted of two parts. Firstly, the attendance of an additional resident during peak hours. Earlier research at the ED of our hospital showed a peak of patients’ visits between 18.00 and 21.00 hours. Unfortunately, during this period the residents changed shifts. Therefore, the first intervention was to add an extra resident at the ED during these peak hours. Secondly, a planning board was installed to enable ED staff to coordinate the care of patients at the ED better. Both interventions reduced DNT slightly to 169 (IQR 120-348) minutes.

2. During discussion meetings it became clear that most residents waited for the laboratory results before examining the patient, which is likely to result in a delay in antibiotic administration. Therefore, the second intervention required residents to immediately examine patients after arrival at the ED. This intervention resulted in a small increase in DNT to 176 (IQR 101 to 250) minutes compared with the DNT after implementation of the first intervention, but still a decrease compared with baseline measurements.

3. Prior analyses of the chest X-ray process showed a 45-minute delay in taking and assessing a chest X-ray at the (external) Radiology Department. So, the third intervention consisted of taking chest X-rays immediately at the ED instead of the Radiology Department. The combined effect of the first three interventions increased DNT to 196 (IQR 138 to 319) minutes.

4. An interim analysis showed a delay in iv antibiotic administration, when administration took place on the ward instead of the ED (*Figure 3*). Therefore, the fourth intervention was to administer all iv antibiotics at the ED instead of the ward. The cumulative effect of the first four interventions resulted in a substantial DNT decrease to 147 (IQR 93 to 207) minutes (p=0.014) when compared with the baseline DNT.

5. The results of the project were discussed with the residents and their supervisors. It became clear that in patients with the suspicion of a severe infection a positive result from a urine analysis was enough to start antimicrobial treatment. Because results of urine analysis done at the ED were available faster than results of blood tests, it was decided to introduce a final intervention: to perform a primary dipstick urine analysis at the ED. By adding this fifth intervention, the DNT showed a slight increase to a median DNT of 155 (IQR 95 to 221) minutes. Finally after all five interventions were implemented the DNT was reduced by 15.3% (p=0.040) when compared with baseline DNT.

**Figure 1. Effect of the interventions on the door-to-needle time in minutes**

**Figure 2. Effect of the interventions on the hospital stay in hours**

Absolute numbers (median, IQR) of all included patients after each new intervention are given. *p=0.14 compared with baseline.*
Additional assessment was carried out one year later at the ED to study whether the interventions still had an effect on the DNT. During a one-month period, we included 35 patients with the same criteria as all the other patients in this project. We found a comparable median DNT of 153 minutes (IQR 109 to 194).

**Hospital Stay and Presentation Time**

*Figure 2* shows the effects of the five implemented interventions on hospital stay (HS). Median baseline HS was 144 hours (IQR 96 to 264) (6 days). After the first, second and third intervention the HS increased to 168 (IQR 96 to 354) hours (7 days), 168 (IQR 108 to 324) and 156 hours (IQR 72 to 402) (6.5 days), respectively. After the fourth intervention HS returned to baseline, namely 144 (IQR 96-288) hours (6.0 days). Finally, after implementation of the fifth intervention the combined effect of all interventions reduced HS to 120 hours (IQR 72-264) (5 days), when compared with baseline HS, leading to a trend towards a significant reduction of HS from 16.7%.

Median DNT appeared to be shorter (145 minutes, IQR 95-201) in patients who arrived at the ED at night (between 17.30 and 20.30 hr) than in patients who arrived during office hours (173 minutes, IQR 118 to 258) (p=0.006).

**Discussion**

The aim of this project was to decrease the door-to-needle time (DNT) and hospital stay (HS) in patients with a severe infection by using tailored interventions. After five tailored interventions, the DNT and HS were reduced by 15.3 and 16.7%, respectively.

Despite availability of treatment guidelines for the most serious infections, the efficiency of the process depends on many factors. Patients arriving at the ED are seen by a multidisciplinary team of professionals in an often busy and chaotic setting. We studied the effect of a reduction in the DNT in patients with a severe infection, not only pneumonia. Previously, it was shown in several studies that a reduction in DNT is possible in patients with pneumonia by using specific interventions. Examples of interventions in these studies are educational interventions. Investigators educated the ED staff about the importance of rapid antibiotic delivery and confronted the staff with long DNT in their hospital. Another example is a multifaceted strategy, in which a steering committee designed a care pathway, based on existing guidelines. The interventions in those studies were implemented using a combination of information packs, interactive group educational sessions, using posters and electronic reminders.

In a comparable project in another Dutch university hospital, Natsch et al. used interventions such as newsletters and lectures to inform the medical staff about the delay in administration of antibiotics and distributed guidelines on managing patients and obtaining cultures. In addition, they improved the availability of antibiotics at the ED and removed financial restraints. These interventions are comparable with the interventions we implemented in our project. As expected, they also found a shorter DNT when the patient was admitted during the night, which is comparable with the results of our project.

Concerning the DNT, Natsch et al. reduced the DNT by 1.8 hours (p=0.04), but started with a longer baseline DNT of 5.0 hours. However, we started with a shorter baseline DNT of 3.0 hours and reduced DNT by 0.47 hours to 155 minutes. Even though our reduction is less spectacular, the final DNT in our project is shorter than reported in earlier research. The literature generally uses a cut-off point of a maximum of four hours concerning DNT. The question remains what minimum DNT is necessary and achievable.

It has been shown that each hour of delay in antimicrobial administration was associated with an average decrease in survival of 7.6%, in patients with a septic shock. However, the number of patients in the present project was too small to do a subanalysis for this specific patient population. After implementation of four out of five interventions, a reduction in DNT was observed in the present project. This fourth intervention stated that all antibiotics had to be given in the ED. This is in concordance with the recently developed guideline for the treatment of community acquired pneumonia in which it is mentioned: the first antibiotic dose has to be administrated while the patient is still at the ED. In our project we noted that not all antibiotic agents were present at the ED and in addition, as a result of our intervention, antibiotics were used in larger doses, which initially resulted in supply problems.
We conclude that only the fourth intervention (antibiotics at the ED) resulted in a clear effect compared with other interventions. The pitfall of DNT reduction, on the other hand, may be that patients at the ED receive doses of antibiotics that are too high, as has been reported for patients with community-acquired pneumonia. Unfortunately, implementing the first three interventions did not really decrease our DNT. This is not due to differences in patients characteristics, since we demonstrated that characteristics of the patients were comparable between the groups. A cumulative effect might have resulted in the decrease after the implementation of the last two interventions. However, our project was not designed to demonstrate the separate effect on the DNT for each intervention. With respect to the secondary outcome parameter HS, it is important to notice that HS is more likely to be influenced by external factors than DNT. For example, difficulties with discharging to nursing homes, because of waiting lists and Christmas holidays. However, implementation of tailored interventions as mentioned can result in a reduction in the DNT and might improve the survival of patients presenting with infections at the ED.

This study was part of a health care innovation project. We included all patients arriving at the ED for a period of nine months. The total number of patients included in this study as well as the distribution between the groups are therefore based on daily practice. In conclusion, cumulative implementation of tailored interventions, especially administrating antibiotics at the ED, results in a reduction of the DNT.

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REFERENCES


