Original Article

What accounts for the delay in antibiotic administration in children with suspected sepsis in the emergency department?—a case control study

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Background: Delay in antibiotic administration is known to increase mortality in patients with sepsis. Our objective was to analyse the determinants of delay of antibiotic administration in children with sepsis.

Methods: A retrospective case record review was conducted over a 6-month period. Included were all children at risk of sepsis. Analysed were time taken from admission to triage, from triage to review by a doctor, from review by doctor to making a diagnosis of possible sepsis, from making this diagnosis to prescribing antibiotics and from prescribing antibiotics to administration. In a retrospective case controls study data were compared on children who received antibiotics within one hour (controls) and more than one hour (cases).

Results: Screened were 90 admissions to a secondary care hospital with suspected sepsis. A total of 53 episodes were included. In 11 (20%) episodes antibiotic administration was done within an hour of admission. Components of the delay were [median (range)] 9 min (range, 0–45 min) from admission to triage, 45 (0–175 min) from triage to being seen by a doctor, 20 min (range, 0–360 min) from seen by doctor to diagnosis of suspected sepsis, 25 min (range, 0–214 min) for time from diagnosis to prescribing and 22 min (range, 3–178 min) from prescribing to antibiotic administration. In patients with a delay of antibiotic administration of more than one hour the delay was significantly associated with an increase in time taken for doctor led management and not related to illness or patient characteristics.

Conclusions: Delayed antibiotic administration in children with suspected sepsis resulted mainly from delayed review by a doctor and delayed antibiotic prescription after diagnosis.

Keywords: Antibacterial agents; sepsis; child

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Introduction

Delay in antibiotic administration is known to increase mortality in patients with sepsis and this has been described for the delay until shock occurs in a prospective study and in hypotensive septic shock retrospectively (1,2). What constitutes this delay is unknown. Our objective was to analyse the determinants in delay of antibiotic administration in children at risk of sepsis. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jeccm-20-74).

Methods

Study design

This was a retrospective case record review over a 6-month period of case records of children. A case control design was applied comparing data on children who received antibiotics within 1 hour of admission and those where there was a delay beyond 1 hour. Ethical approval or consent was not required for this service audit project. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Setting

The setting was a dedicated paediatric emergency department and paediatric assessment unit of a municipal district general hospital in the United Kingdom. A sepsis pathway designed according to guideline 51 of the National Institute of Health and Care Excellence of the United Kingdom (3) alerting all staff to features and required rapid management of sepsis is in place. All staff is aware of this pathway which is taught and adherence audited regularly. Electronic patient records were analysed for all consecutive children up to 16 years of age seen over a 6 months period between beginning of July and end of December 2017 fulfilling the inclusion criteria (see below). The time intervals relating to diagnosis and decisions between admission and antibiotic administration were analysed and related to patient characteristics.

Participants

Inclusion criteria: Included were all children with suspected sepsis on admission as defined according to an agreed pathway as fever above 38 or looking sick or parent/carer very worried or has the paediatric early warning system (4) triggered and where data were complete in documentation of time of admission, time of triage, time seen by doctor, time of diagnosis with decision to treat, time of prescription of antibiotic and time of administration of antibiotic.

Exclusion criteria

All children where the clinician did not suspect sepsis or there was no documentation of any of the time points mentioned in the inclusion criteria.

Variables

The time intervals between those time points were analysed and compared. Data extraction for all included children was done on an excel spreadsheet (Microsoft word). Documented were gender, age, seniority of doctor involved before antibiotic administration, oxygen saturation, body temperature, heart rate, Pediatric Early Warning System (PEWS) Score (Paediatric Early Warning System score is calculated from the following parameters: General appearance, capillary refill time, heart rate deviation from the norm, work of breathing, deviation of respiratory rate from the norm, oxygen or nebuliser requirements and presence of vomiting), C-reactive protein and lactate level and as predictors, confounders and modifiers of outcome final microbiological result, final diagnosis, duration of antibiotic course administered, type of antibiotic administered and as outcomes death and long term sequelae.

Data sources/measurement

All data were extracted from electronic patient records retrospectively and transferred onto an Excel spread sheet (Microsoft word) and from there data were for statistical analysis after anonymization imported into SPSS version 20 (IBM) for analysis.

Bias

To reduce bias and confounding by severity of disease in investigation of delay of antibiotic administration Pediatric Early Warning Score, temperature, heart rate, lactate, C-reactive protein on admission and duration of antibiotics were recorded. To reduce bias due to the final diagnosis being a viral illness this was recorded and compared between cases with and without delay of antibiotic administration beyond one hour.

Study size

Due to lack of previous studies on this topic a sample size calculation was not possible and the project was a piloting audit to explore where the likely delays in antibiotic administration are in order to inform a sample size calculation for future audits.

Quantitative variables

Compared were data on children who received antibiotics within 1 hour of admission and those where there was a delay beyond 1 hour. The 1-hour cut-off was chosen because previous research (1) revealed that each hour delay of antibiotic administration in septic shock was associated with an increase in mortality. The time interval between seen by doctor and time of prescription by the doctor

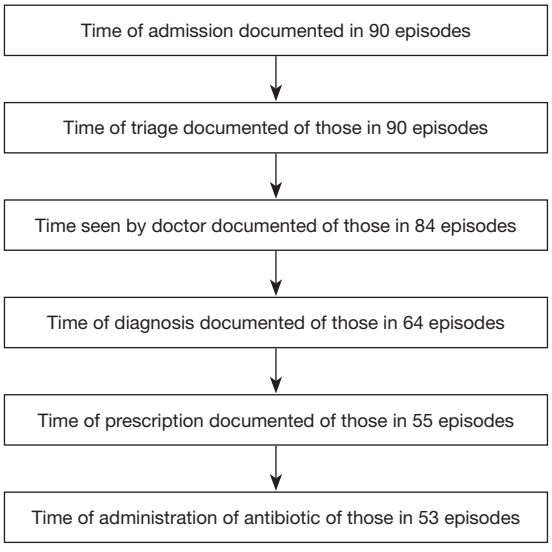

Figure 1 Flow chart of drop outs due to incomplete data.

Table 1 Time line from admission to antibiotic administration (n=53)

Time intervals	Duration, min [median (range)]
Time from admission to triage	9 (0 to 45)
Time from triage to seeing a doctor	45 (0 to 175)
Time from seen by doctor to diagnosis of suspected sepsis	20 (0 to 360)
Time from diagnosis to prescribing	25 (0 to 214)
Time from prescribing to antibiotic administration	22 (3 to 178)
P value (Kruskal-Wallis test)	<0.001*

*, on post-hoc analysis the time interval from admission to triage compared to all other time intervals individually was statistically significantly different.

was taken as doctor led management and the other time intervals: time between admission and seen by doctor and between time of prescription to time of administration by nurse as nurse led management and the proportion of the total delay attributable to medical and nursing time compared between groups.

Statistical methods

For analysis of differences between components of the delay in antibiotic administration the Kruskal-Wallis test for multiple comparison was used. For comparison of patients with a delay of antibiotic administration of more than an hour and less than an hour and C-reactive protein levels the Mann-Whitney U test was used for comparison of age, duration of antibiotic treatment and PEWS score and the *t*-test for body temperatures heart rate, lactate levels. Chi-square or Fishers exact test were used as appropriate for sex, seniority of involved doctors, percentage of delay due to involvement of medical versus nursing staff, organisms isolated and final diagnosis. A two tailed P value of <0.05 was taken as indicating a statistically significant difference.

Results

Participants

Screened were 90 episodes of admissions to a secondary care hospital with suspected sepsis. A total of 53 episodes were included; 37 episodes were excluded because data on timing of admission, time of triage, time seen by doctor, time of decision to treat, time of prescription of antibiotic or time of administration of antibiotic was missing (*Figure 1*). In 11 (20%) episodes antibiotic administration was done within an hour of admission.

Descriptive data

According to guideline 51 of the National Institute of Health and Care Excellence of the United Kingdom (3) 32 episodes were at high risk of sepsis, 4 at moderate and 17 at low risk. There was no difference in delay of antibiotic administration between groups of differing risk: for patients with high risk it had a median (range) of 173 min (range, 26–488 min), with moderate risk 236 min (range, 32–293 min) and low risk of 163 min (range, 27–481 min) (Kruska-Wallis test P=0.624). The components of the delay in antibiotic administration are shown in *Table 1*. The comparison of personal characteristics of patients and management comparing patients with a delay less than to greater than an hour is shown in *Table 2*. None of the patients included had oxygen saturations of less than 94% on admission. All but three patients (who received benzylpenicillin, piperacillin or vancomycin) received intravenous ceftriaxone or cefotaxime. All patients survived the illness episode and without known long term sequelae.

Outcome data and main results

The mean delay (SD) from admission to antibiotic

Table 2 Personal characteristics of patients with suspected sepsis and management comparing patients with a delay in antibiotic administration of less than to greater than an hour

Personal characteristics and management	Delay 1 hour or less (n=11)	Delay of more than 1 hour (n=42)	P value
Age (months), median (range)	12.0 (0.25 to 24)	3.5 (0.35 to 72)	0.136
Sex (female), n (%)	2 (18.1)	15 (35.7)	0.469
PEWS score* on admission, median (range)	3 (0 to 5)	1(0 to 5)	0.115
Temperature on admission (℃), mean (SD)	37.8 (1.44)	38.1 (0.96)	0.371
Heart rate on admission, mean (SD)	161 (35.0)	160 (24.0)	0.975
Lactate on admission (mmol/L), mean (SD)	3.5 (0.10)	2.3 (0.18)	0.117
C-reactive protein level on admission (mg/L), median (range)	25.17 (0.6 to 151.30)	33.74 (0.6 to 206.0)	0.623
Number of patients with pathogenic bacteria isolated from sterile sites, n (%)	2[#] (18.1)	6[&] (14.2)	0.665
Final diagnosis on discharge an illness other than sepsis, n (%)	3[$] (27.2)	13[$] (30.9)	1.000
Duration of antibiotic treatment (hours), median (range)	72 (24 to 336)	72 (24 to 168)	0.785
Experienced trainee (registrar level) involved before antibiotic administration, n (%)	6 (54.5)	36 (85.7)	0.064
Consultant involved before antibiotic administration, n (%)	2 (18.1)	5 (11.9)	0.625

*, PEWS score = Paediatric Early Warning System score calculated from the following parameters: general appearance, capillary refill time, heart rate deviation from the norm, work of breathing, deviation of respiratory rate from the norm, oxygen or nebuliser requirements and presence of vomiting. [#], Neisseria meningitides in cerebrospinal fluid: 1; *Escherichia coli* (*E. coli*) coli in a blood culture: 1. [&], group A streptococcus in blood culture: 1; *E. coli* in urine: 2 (one also had *E. coli* in the blood culture and only one site was counted in the table; *E. coli* in blood culture: 3; Neisseria meningitidis in CSF: 1. [$], final diagnoses were viral illnesses including viral respiratory tract infections, gastroenteritis, and enterovirus meningitis.

administration if it lasted an hour or less was 41 min (SD 10) with 33 min (SD 79%) accounted for by nursing interventions and 8.5 min (SD 20%) by doctor intervention and in episodes where the delay was more than an hour it was 212 min (SD 106) with 95 min (SD 52) or 45% accounted for by nursing interventions and 117 min (SD 90) or 54% by doctors interventions. The increase in percentage of time spent during the doctors' intervention in episodes where there was a delay in antibiotic administration of more than an hour was significant (Chi-square test, P<0.001).

Discussion

Key results

This is the first study analysing the components constituting the delay in antibiotic administration in children with a diagnosis of possible sepsis. The study identified easily avoidable delays including time until seen by a doctor and time from diagnosis to prescription of an antibiotic. There was no evidence of a relationship of a more rapid management of patients with suspected sepsis with risk of sepsis, final confirmed sepsis diagnosis or disease severity or seniority of doctor involved before antibiotic administration. The overall delay in antibiotic administration to more than an hour was mainly attributable to an increased time for the intervention by the doctor and between being seen and the antibiotic prescribed. Training nurses to do prescribing and pre-prescribed antibiotics as part of a sepsis care bundle may reduce this delay in situations of doctor shortage.

Limitations

Limitations of this case control study include that the degree of proficiency in application of the sepsis pathway amongst doctors and the doctor/patient ratio was not known and may have influenced the time interval until seen by the doctor and time interval from sepsis diagnosis to antibiotic prescribing.

Interpretation

The delay between triage and being seen by the doctor, which was in absolute terms the biggest part of the overall delay in antibiotic administration could be shortened by training nurses at the point of triage to make the diagnosis following agreed pathways as outlined in national guidance (3) enabling them to alert doctors early and by training paramedics to pre-alert hospital staff during ambulance transfer. Delayed antibiotic administration in children with suspected sepsis resulted mainly from delayed review by a doctor and delayed antibiotic prescription after diagnosis.

Generalisability

Future larger studies in different settings (e.g., in a low-income country) need to check whether the results of this pilot study are reproducible in settings of different availability of medical and nursing staff and different levels of competencies of nursing staff, which in our setting were unable to prescribe antibiotics.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/jeccm-20-74

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jeccm-20-74). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Ethical approval or consent was not required for this service audit project. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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