Original Article

A survey of emergency physicians' prescription of piperacillin/tazobactam

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ABSTRACT

INTRODUCTION. Piperacillin/tazobactam (Pip/Taz) is a broad-spectrum antibiotic, often prescribed in emergency departments (EDs). Excessive use of broad-spectrum antibiotics may lead to the rise of antimicrobial resistance, a concerning health issue. We investigated physicians' adherence to regional guidelines and their considerations when prescribing Pip/Taz in the ED.

METHODS. In this cross-sectional survey, a ten-item survey questionnaire was administered to ED physicians in five EDs from 10 January to 7 February 2024.

RESULTS. A total of 261 physicians employed in the ED were invited to participate in the survey. Among these, 144 physicians completed the survey, yielding a response rate of 55.2%. Based on the results, 25% were unaware of the regional guidelines on the prescription of Pip/Taz. In addition, over the past month, 25% had prescribed Pip/Taz in situations where regional guidelines recommended a narrow-spectrum antibiotic, primarily because of concerns regarding the patient's condition (74.3%); 30.6% of those who deviated from guidelines were consultants.

CONCLUSIONS. This study found that a fourth of physicians in EDs were unaware of regional guidelines for prescribing Pip/Taz. Moreover, one in every four physicians purposely deviated from the recommended type of antibiotics, mainly because of concerns about the patient's clinical condition.

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According to the World Health Organization, around ten million people will die annually from drug-resistant diseases by 2050 if no action is taken [1]. Misuse and overuse of antibiotics, particularly broad-spectrum antibiotics, increase the prevalence of resistant microorganisms [2, 3]. Moreover, widespread antibiotic use in livestock production significantly contributes to the development of resistance [4]. There are large global differences in the development of antibiotic resistance. This study was conducted in a low-resistant country [5].

Piperacillin/tazobactam (Pip/Taz) is a broad-spectrum antibiotic often used in emergency departments (EDs) [6, 7]. In addition to being used in cases of serious infections and sepsis, Pip/Taz is often included as part of empirical treatment, even though a more narrow-spectrum antibiotic should be prescribed after diagnostic workup. Restricting the use of Pip/Taz to situations in which it is specifically recommended could contribute to slowing the spread of antibiotic resistance [8, 9].

The Antimicrobial Stewardship programmes aim to ensure the prudent use of antibiotics to reduce the development of antimicrobial resistance (AMR). Various interventions exist, e.g. intravenous to oral conversion,

formulary restrictions and various guidelines [10, 11]. There are regional guidelines for antibiotic treatment to reduce the risk of inappropriate or unnecessary treatment with Pip/Taz. While numerous studies have investigated the development of AMR, no studies have been published on ED physicians' considerations when prescribing Pip/Taz. Therefore, the primary aim of this study was to investigate physicians' adherence to guidelines. Additionally, to explore their considerations when prescribing Pip/Taz.

Methods

Study design

This cross-sectional study employed a questionnaire to explore physicians' considerations prior to prescribing Pip/Taz. The study was reported in accordance with the Equator Network Checklist for Reporting of Survey Studies (CROSS) (Supplementary Figure S1).

Setting and respondents

The setting for this study was five Danish EDs, as they are often the firstplace where Pip/Taz is prescribed. In the Central Denmark Region, there are four regional hospitals: Regional Hospital Gødstrup, Regional Hospital Horsens, Regional Hospital Randers, Regional Hospital Viborg and a single university hospital; Aarhus University Hospital. The following ED physicians were invited to participate in the study: senior registrars, consultants and physicians in postgraduate medical training, residency or fellowship. Accounting for clinical experience, the latter were divided into two groups: < 2.5 years and 2.5-5 years of experience. Only physicians employed in one of the five EDs were included.

Questionnaire

A ten-item questionnaire was developed for this study. Items 1-4 covered sex, age, hospital affiliation and clinical position. Item 5 was a rule-in/out question; respondents who had not prescribed Pip/Taz in the past month were excluded to minimise recall bias. Items 6-7 addressed knowledge and use of regional guidelines, and item 8 assessed guideline adherence. Depending on responses to item 8, participants received either item 9A ('yes') or 9B ('no/don't know'). Item 10 allowed for additional comments. The questionnaire included multiple-choice, Likert scale, yes/no and open-ended questions. Full content is provided in Supplementary Figure S2.

Nine physicians who did not work in EDs but had experience prescribing Pip/Taz pilot tested the questionnaire. They were asked to provide comments regarding the comprehensiveness of the questions and whether any questions were missing or redundant. Based on their comments, some minor changes were made.

Data collection

The questionnaire was created and managed using Research Electronic Data Capture tools (REDCap) at Aarhus University [12, 13] and forwarded to the chief physicians in the included EDs, who distributed it to physicians using their work e-mail. The survey was conducted from 10 January to 7 February 2024. The physicians had a total response time of four weeks and received weekly reminders.

Analysis

Data were analysed with Stata 17.0 (StataCorp, Texas, USA) using descriptive statistics. Categorical and binominal data were reported as numbers and percentages, whereas median and IQR were used for non-normally distributed data.

Qualitative methods

The first and second authors (SDM and SS) categorised open-ended questions independently. First, each

questionnaire response was coded individually. Second, the responses were discussed and divided into logical themes and sub-themes. The open-ended questions were grouped into five overall categories and ten additional sub-themes [14].

Ethical considerations

The questionnaire and information about the study's purpose were sent by e-mail. Respondents answered voluntarily, and completing the questionnaire was considered consent for participation in this study. Data were stored in REDCap and treated confidentially and anonymously.

Trial registration: not relevant.

Results

Study population

A total of 261 physicians employed in EDs were invited to participate in the survey. Of these, 159 returned a completed questionnaire. Four respondents were excluded because they did not meet the inclusion criteria, and six were removed due to incomplete questionnaires, leaving 149 responses. Subsequently, five responses were excluded, as the physicians had not prescribed Pip/Taz in the past month, resulting in a final population of 144 respondents and a total response rate of 55.2% (Supplementary Figure S3).

As shown in **Table 1**, 108 (75%) of the physicians were aware of the regional guidelines for prescribing Pip/Taz. No physicians followed the regional guidelines less than half the time, and 79 (73.2%) followed the guidelines more than half of the time. In addition, 36 (25%) of respondents had prescribed Pip/Taz in the past month, despite guidelines recommending narrow-spectrum antibiotics in the given situation.

TABLE 1 Characteristics of the study respondents, including their prescription of piperacillin/tazobactam (Pip/Taz) and knowledge of guidelines in the emergency departments (N = 149).

Sex, n (%)	
Male	71 (47.7)
Female	78 (52.3)
Age, median (IQR) [minmax], yrs	33 (29-49) [27-67]
Hospital affiliation, n (%)	
A = Regional Hospital Gødstrup	43 (28.9)
B = Regional Hospital Horsens	29 (19.5)
C = Regional Hospital Randers	19 (12.8)
D = Regional Hospital Viborg	33 (22.1)
E = Aarhus University Hospital	25 (16.7)
Clinical position, n (%)	
Postgraduate medical training	43 (28.9)
Resident	17 (11.4)
Fellowship:	
1st half	28 (18.8)
2nd half	15 (10.1)
Senior registrar	12 (8.0)
Consultants	33 (22.1)
Unclassified	< 5 (< 3.4) ^a
How often have you prescribed Pip/Taz within the past month?, n (%)	
Every shift	26 (17.5)
Several times a week	65 (43.6)
Weekly	42 (28.2)
Rare	11 (7.4)
Never ^b	5 (3.3)
Do you have knowledge of the regional guidelines for prescribing Pip/Taz?, n (%)°	
Yes	108 (75)
No	36 (25)
To what extent do you follow the regional guidelines when prescribing Pip/Taz?, $n (\%)^d$	
All the time	20 (18.5)
> ½ the time	79 (73.2)
½ the time	9 (8.3)
< ½ the time	0
Hardly ever	0
Never	0
Have you prescribed Pip/Taz within the past month despite the regional guidelines recommending narrow-spectrum antibiotics?, n (%)c	
Yes	36 (25)
No	77 (53.5)
Do not know	31 (21.5)
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a) Fields with < 5 responses were anonymised.

Table 2 shows that 11 (30.6%) of the respondents who answered "yes" to having prescribed Pip/Taz despite contrary guidelines were consultants. For both physicians in postgraduate medical training, fellowship (second half) and senior registrar, the number who had deviated from the guidelines was < 5 (< 13.3%). A total of 25 (32.9%) of the physicians in postgraduate medical training had not deviated from the guidelines, and 13 (41.9%) answered that they did not know whether they had deviated from the guidelines.

b) Respondents who had not prescribed Pip/Taz within the past month were automatically excluded from the questionnaire at this point.

c) N = 144

d) N = 108.

TABLE 2 Association between prescription of piperacillin/tazobactam within the past month despite regional guidelines recommending a narrow-spectrum antibiotic and physicians' characteristics $(N = 143)^a$.

	Yes (N _y = 36)	No (N _n = 76)	Do not know $(N_d = 31)$
Sex, n (%)			
Male	18 (50)	36 (47.4)	15 (48.4)
Female	18 (50)	40 (52.6)	16 (51.6)
Clinical position, n (%)			
Postgraduate medical training	< 5 (< 13.9)b	25 (32.9	13 (41.9)
Resident	8 (22.2)	6 (7.9)	< 5 (< 16.1) ^b
Fellowship:			
1st half	7 (19.4) 15 (19.7)		5 (16.1)
2nd half	< 5 (< 13.9)b	11 (14.5)	0
Senior registrar	< 5 (< 13.9)b	5 (6.6)	< 5 (< 16.1)b
Consultants	11 (30.6)	14 (18.4)	6 (19.4)
Age, n (%)			
25-34 yrs	17 (47.2)	46 (60.5)	19 (61.3)
35-50 yrs	13 (36.1)	21 (27.6)	5 (16.1)
> 50 yrs	6 (16.7)	9 (11.9)	7 (22.6)

a) 1 dropout due to non-response to the above.

Considerations

As shown in **Table 3**, a total of 36 (25%) physicians answered "yes" to having prescribed Pip/Taz in the ED within the past month, even though regional guidelines recommended narrow-spectrum antibiotics. The vast majority (26, 74.3%) stated that they did so because they were worried about the patient's condition (e.g., suspected sepsis or deterioration of vital signs), five (14.3%) were following colleagues' recommendations and < 5 (< 14.3%) chose the option "other".

b) Fields with < 5 responses were anonymised.

TABLE 3 Reasons why the physicians prescribed piperacillin/tazobactam (Pip/Taz) despite the regional guidelines recommending narrow-spectrum antibiotic (N = 35)^a.

What was the reason why you prescribed Pip/Taz despite the regional guidelines recommending narrow-spectrum antibiotics?

n (%)

•	(, , ,
"I was worried about the patient's condition" (e.g. suspected sepsis or deterioration of vital signs)	26 (74.3)
"I consulted a colleague about the patient who recommended Pip/Taz"	5 (14.3)
Other ^b	< 5 (< 14.3)
"I usually prescribe Pip/Taz"	0
"I felt pressured to prescribe, for instance due to time pressure"	0
"The nurse recommended me to prescribe Pip/Taz"	0
"I was in doubt as to what to choose"	0
"Patient/relative requested treatment with Pip/Taz"	0

- a) 1 dropout due to non-response to the above.
- b) Includes, among others, medicine shortages, easier to administrate Pip/Taz, guidelines do not take microbiological or radiological findings into account.

Meanwhile, 108 (75%) physicians answered "no" or "don't know" when asked about prescribing Pip/Taz in the past month. Among these, 83 (40.9%) stated that the patient met the criteria for Pip/Taz, 66 (32.5%) were concerned about the patient's condition, 43 (21.2%) followed colleagues' advice, and 11 (5.4%) selected other options from the questionnaire. Results from item 9B are presented in Supplementary Table S1.

Other comments

A total of 35 (24.3%) physicians used the opportunity to provide other comments, producing 47 different quotes (some provided more than one comment). The comments were categorised into five overall themes and ten subthemes (**Table 4**).

TABLE 4 Overview of quotations related to physicians' prescription of piperacillin/tazobactam (N = 47)

Overall theme	n (%)	Sub-theme	Supporting quotations
Quick treatment 15 (31.9)	Acutely ill patients in need of rapid initiation of treatment	"Pip/Taz is often prescribed in the ED, but I think most of all that it is due to the fact that most patients are unwell/septic and require urgent/quick antibiotic treatment, and there is Pip/Taz, after all, the gold standard for sepsis" "I experience a tendency towards quick use, myself incl., in patients with worrisome/threatening vital signs or generally, worrying situations"	
		Unknown focus	"If the patients are undecided and you want to start treatment quickly, you often choose Pip/Taz" "Often due to doubts about the focus, e.g., both suspected urinary tract infection and respiratory tract infection
Ambiguities and 12 (25.5) differences	Differences in prescribing behaviour among hospitals and between departments	"It is my experience that the medical physicians are better at the various treatment guidelines in relation to the choice of antibiotics, so they are often better to confer with in the first place. Emergency physicians on call do very often recommend Pip/Taz" "Standard from departments to which we send patients: oncology, orthopaedic surgery, urology and gastrointestinal surgery departments"	
	Ambiguities about guidelines or definitions	"Sometimes it is difficult to distinguish between moderate and severe pneumonia. The guidelines are not easy to interpret" "The regional guideline is difficult to find in E-dok [electronic patient record with regional guidelines]. It must be made more visible and easier to find. In addition, reading the receipt is a good way to secure information"	
Medicine shortages	8 (17.0)	Medicine shortage for intravenous treatment of urosepsis/urinary tract infections/pyelonephritis	"Cf. guidelines regarding pyelonephritis/urosepsis, too much Pip/Taz is used due to delivery problems with other antibiotics" "A problem is other types of antibiotics on back order, e.g. intravenous selexid, which unfortunately means that an alternative is Pip/Taz"
Overtreatment 6 (12.8)	Pip/Taz is prescribed to be on the safe side	"It is generally given too often when other intravenous antibiotics could be chosen, for example ampicillin/ gentamycin or cefuroxime for upper urinary tract infections" "It is prescribed as a 1-time prescription to be on the safe side. It is very worrying"	
		Prescribed too often	"We prescribe far too much Pip/Taz. Furthermore, I find that several physicians have started to prescribe Pip/ Taz × 4 daily, currently without septic shock, which I believe is a clear overtreatment" "Sometimes I experience a tendency to quickly recommend Pip/Taz where you could consider waiting with antibiotics"
Pressure 6 (12.8)	6 (12.8)	Insufficient time for supervision	"In the ED, Pip/Taz is often prescribed due to pressure of time. As the youngest physician, you often just do as the more experienced physicians say, because there is not always time for explanation"
		Younger physicians	"I think that far too much Pip/Taz is prescribed because there are many younger physicians in an ED. I think they choose Pip/Taz because it is the safe choice, so it is probably based on uncertainty among the physicians"
		Time pressure	"My clear thought is that Pip/Taz is prescribed quite a bit in the ED, and probably also quite a bit too much, as we often are worried about the patient, are a little uncertain about the focus of infection and it is ,easier in a busy workday if we are in doubt about the right choice of antibiotic" "If the medical record is a little more thorough, there will be a less prescription of Pip/Taz"

Discussion

In this study, we investigated emergency physicians' adherence to guidelines and their considerations when prescribing Pip/Taz. We received 144 responses, of which 25% of the respondents had prescribed Pip/Taz within the past month despite guidelines recommending that they prescribe a more narrow-spectrum antibiotic. Concerns for the patients were the main consideration for deviating from the guidelines (74.3%).

Nearly 90% of respondents prescribed Pip/Taz at least once a week, with 17.5% prescribing it during every shift. Additionally, 25% were unaware of the regional guidelines, potentially leading to inappropriate prescribing of Pip/Taz. This aligns with a Danish study, which found that only 31.3% of patients were treated according to regional guidelines [15]. To address this, EDs could emphasise the importance of guideline knowledge, e.g., by using read-receipt e-mails to ensure that important information is received.

In our study, 25% of physicians deviated from guidelines with patient concern as the primary reason. Concerns for patients also contributed to the unnecessary use of broad-spectrum antibiotics rather than narrow-spectrum antibiotics as empirical treatment in a study from the Netherlands [16]. Additionally, 14.3% of those deviating from guidelines had consulted a colleague, which may be particularly prevalent among younger ED physicians. Some respondents noted that older physicians often recommend Pip/Taz, despite it being inappropriate, likely due to time pressure limiting their ability to provide adequate supervision. A study from the UK found that younger physicians are often reluctant to challenge the prescribing practices of their older colleagues, even if they disagree [17]. Another study revealed that a hierarchical structure within departments leads younger physicians to passively accept prescriptions out of fear of criticism or the burden associated with taking individual responsibility for the patient [18]. The findings suggest a need for improved supervision of younger

physicians, e.g., by ensuring easier access to a consultant in the EDs.

We examined the association between clinical position and prescribing Pip/Taz despite guidelines recommending narrow-spectrum antibiotics. Physicians in postgraduate medical training were least likely to prescribe Pip/Taz, whereas consultants and residents were more likely. A UK study found that younger physicians followed guidelines more often than consultants, who relied on their gut feeling, leading to more deviations [17]. Consultants, who have more experience, may prescribe Pip/Taz based on past practice rather than guidelines - "we usually" prescribe Pip/Taz in this situation. Increased clinical demands and patient responsibility during residency may also drive physicians to prescribe Pip/Taz to "play it safe." A study from London showed that clinicians' concerns about patients influenced their prescription of antibiotics and that their use of antibiotics was tied to a belief that antibiotics would protect patients from deterioration and themselves from the ethical consequences of undertreatment [19]. One suggestion from a respondent was to allocate more time for a thorough medical history, which could reduce unnecessary use of Pip/Taz.

Among those who answered "don't know" to adhering to guidelines for prescribing Pip/Taz, four of ten were physicians in postgraduate medical training. This highlights the need for better access to guidelines in EDs. We also received feedback about ambiguities in guidelines, e.g. regarding sepsis, and the lack of consideration for patients' clinical conditions (e.g., microbiological or radiology findings). A study from the Netherlands found that barriers to guideline adherence included poor understanding, making it more difficult to accomplish adherence [16]. Recent research has shown that easily accessible, high-quality guidelines may reduce broad-spectrum antibiotic use in EDs, promoting more prudent prescribing patterns [20]. Guidelines should therefore be presented in formats that are quick and easy to use, given the time pressures that ED physicians face. They should be short, precise and unambiguous - but also allow room for clinical judgement, recognising that one size does not fit all, and that personalised medicine may require deviations from guidelines in certain situations.

Strengths and limitations

A strength of this study is the high response rate of 55.2% and the well-distributed characteristics and levels of experience.

The study also has some limitations. First, when using a questionnaire focusing on events and decisions made in the past, there is a risk of recall bias, though this was minimised using a rule-out question. Second, we also used a self-constructed questionnaire, as no validated Danish version existed for examining physicians' adherence to guidelines and considerations when prescribing Pip/Taz. The questionnaire was pilot-tested and found suitable. Third, categorising free-text comments into themes was based on individual assessments by the first and second authors (SDM and SS). The process followed the recommendations for thematic analysis, with each assessor individually reading and analysing the comments and suggesting themes. Subsequently, the suggested themes were compared, and decisions on the final themes were made. Fourth, we observed an inconsistency regarding the question about knowledge of the regional guidelines. Lastly, we observed inconsistency regarding understanding regional guidelines: 25% claimed not to be aware of them, but all reported following them at least half the time, suggesting possible over-reporting of guideline use.

The findings in this study must be interpreted in relation to the above-mentioned limitations. The findings, which were largely in line with those of international studies, may be applicable to other regions in Denmark and possibly to EDs in other countries with comparable healthcare settings.

Conclusions

This study examined physicians' adherence to guidelines and considerations for prescribing Pip/Taz in EDs. We

found that a fourth of physicians in EDs were unaware of regional guidelines for prescribing Pip/Taz. Moreover, one in every four physicians purposely deviated from the recommended type of antibiotics, mainly because of concerns about the patient's clinical condition.

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