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Original article

Sequential oral antibiotic in uncomplicated *Staphylococcus aureus* bacteraemia: a propensity-matched cohort analysis

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ABSTRACT

Objectives: We aimed to analyse the efficacy and safety of oral sequential therapy (OST) in uncomplicated *Staphylococcus aureus* bacteraemia (SAB).

Methods: Single-centre observational cohort at a tertiary hospital in Spain, including all patients with the first SAB episode from January 2015 to December 2020. We excluded patients with complicated SAB and those who died during the first week. Patients were classified into the OST group (patients who received oral therapy after initial intravenous antibiotic therapy [IVT]), and IVT group (patients who received exclusively IVT). We performed a propensity-score matching to balance baseline differences. The primary composite endpoint was 90-day mortality or microbiological failure. Secondary endpoints included 90-day SAB relapse.

Results: Out of 407 SAB first episodes, 230 (56.5%) were included. Of these, 112 (n = 48.7%) received OST and 118 (51.3%) IVT exclusively. Transition to oral therapy was performed after 7 days (interquartile range, 4–11).

The primary endpoint occurred in 10.7% (11/112) in OST vs. 30.5% (36/118) in IVT ($p < 0.001$). SAB relapses occurred in 3.6% (4/112) vs. 1.7% (2/118) (p 0.436). None of the deaths in OST were related to SAB or its complications.

After propensity-score matching, the primary endpoint was not more frequent in the OST group (relative risk, 0.42; 95% CI, 0.22–0.79). Ninety-day relapses occurred similarly in both groups (relative risk, 1.35; 95% CI, 0.75–2.39).

Discussion: After an initial intravenous antibiotic, patients with uncomplicated SAB can safely be switched to oral antibiotics without apparent adverse outcomes. This strategy could save costs and complications of prolonged hospital stays. Prospective randomized studies are needed. **Itziar Diego-Yagüe, Clin Microbiol Infect 2023;■:1**

Introduction

Staphylococcus aureus bacteraemia (SAB) is one of the most common causes of bacteraemia. It has an estimated incidence of 15 to 40 cases per 100 000 persons/year, with a mortality rate >20% [1].

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In patients with uncomplicated SAB, current guidelines recommend ≥14 days of intravenous antibiotic therapy (IVT) [1–3]. Recent surveys of experts in the treatment of this infection show that many would not consider the transition to oral antibiotics, even after good response [4,5].

However, prolonged IVT can lead to greater complications and costs derived from longer hospitalization. Hence, oral sequential therapy (OST) would allow saving on hospital stays and avoiding these complications. Although OST has been widely studied in other types of bacteraemia [6–9], in uncomplicated SAB, there is little evidence to support it. Consequently, it has recently been proposed that the study of OST in uncomplicated SAB is one of the highest research priorities in this infection [10].

The aim of this study was to analyse the efficacy and safety of OST in uncomplicated SAB.

Patients and methods

We performed a single-centre observational cohort study. Puerta de Hierro University Hospital is a tertiary care hospital in Madrid (Spain) with 613 beds and a target population of 550 000 patients.

From January 2015, all patients aged >18 years with a monomicrobial first positive blood culture (BC) (index BC) for SA were prospectively included in a microbiological database. For this study, we included patients up to December 2020.

Information regarding the variables under study was manually extracted from the electronic medical record. An anonymized predesigned data collection form (.xlsx format) was used. Demographic information, comorbidities, clinical, primary focus, microbiological, complementary tests, antibiotic management, and follow-up were included.

Patients with complicated SABs were excluded. To mitigate survivor bias, patients who had died within the first 7 days from the collection of the index BC were excluded.

The patients finally included were classified into two groups: Group 1 (OST) included patients who received ≥48 h of oral therapy after an initial IVT; Group 2 (IVT) included patients who received either exclusively IVT or <48 hours of oral therapy.

BC was processed using the BD BACTEC FX system (Becton Dickinson, Sparks, MD, USA). When positive, the strain was identified using the MALDI-TOF system (Brucker Daltonic). All processing was performed according to the manufacturer's instructions.

Definitions

Uncomplicated SAB was defined as that which did not meet complication criteria according to the Infectious Diseases Society of America (IDSA) and Sociedad Española de Infecciosas y Microbiología Clínica (SEIMC) guidelines [1,4]. These criteria include positive control BC or persistence of fever after 72 hours of adequate treatment, evidence of endocarditis, thrombophlebitis, or other endovascular infections, evidence of septic embolism, evidence of osteoarticular infection, and absence of adequate focus control or presence of cardiac valve prostheses.

Endocarditis was defined according to the modified Duke criteria [11]. Persistent bacteraemia was defined as the presence of positive control BC after 72 hours of effective antibiotic therapy. Nosocomial bacteraemia was classified as bacteraemia during hospitalization and with the onset of symptoms at least 48 hours after admission. Healthcare-associated bacteraemia (HAB) was defined as a bacteraemia occurring during the 90 days after hospital discharge or in patients with extensive healthcare contact (including haemodialysis, intravenous chemotherapy, chronic ulcers with treatment in healthcare centres, and invasive procedures). These bacteraemias that did not meet the nosocomial or HAB criteria were classified as community-acquired bacteraemia. Primary bacteraemia was defined as that without an apparent clinical focus. Adequate control of the focus was defined as the removal of vascular catheters suspected of being the origin, removal of infected prosthetic devices, or drainage of infected collections. In the absence of vascular catheters, infected prosthetic devices, or drainable collections, the focus was considered adequately controlled. Microbiological failure was defined as isolation of an undistinguishable SA from a sterile sample beyond the 14th day of antibiotic treatment, in accordance with the proposed definition [12]. Relapse was defined as isolation of an undistinguishable SA from a blood sample beyond the 14th day of antibiotic treatment. All-cause hospital readmission was defined as the need for a new hospital admission by any cause after an initial discharge. SAB-related mortality was defined as death that the treating physician considered directly related to SAB. SAB-related hospital readmission was defined as a new hospital admission due to a complication of the initial SAB (including complications of its treatment), a SAB relapse, or microbiological failure.

Primary and secondary outcomes

The primary endpoint was the proposed-consensus outcome at 90 days [12], which was a composite of 90-day all-cause mortality and 90-day microbiological failure. Secondary endpoints included 30-day mortality, 90-day relapse, 90-day mortality, SAB-related 90-day mortality, all-cause 90-day hospital readmission, SAB-related 90-day hospital readmission, and occurrence of serious adverse effects requiring hospital admission or discontinuation of antibiotics.

Statistical analysis

Qualitative variables were expressed as percentages and absolute values. Continuous variables were expressed as medians and interquartile ranges (IQR). Differences in baseline and clinical characteristics of the patients were evaluated with Mann-Whitney's U test for continuous variables and with the chi-square test (or Fisher's exact test when necessary) for qualitative variables.

To balance the differences in the characteristics between the two groups, a propensity score (PS) matched analysis was performed according to current recommendations [13,14]. These variables with significant differences between the two groups and potentially associated with mortality were chosen to create the PS: arterial hypertension, previous heart failure, SOFA score, primary bacteraemia, or methicillin-resistant SA. A 1:1 PS matching without replacement and with calliper of 0.05 was performed, creating the PS-matched cohort (PSc). The correct balance of baseline characteristics was verified by means of a univariate analysis similar to that aforementioned.

Primary and secondary endpoints were assessed by the chi-square test, providing relative risks and their 95% CIs.

Bilateral exact p values of <0.05 were considered statistically significant differences. All analyses were performed using SPSS software (version 26.0; SPSS, Inc).

Ethics

The study was approved by the hospital ethics committee. Because this was a retrospective, non-interventional study that only required the collection of previously generated and anonymous data, informed consent was not required.

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Results

Out of a total of 407 SAB first episodes, 250 (61.4%) were classified as uncomplicated SAB, and 20 patients (8.0%) died within the first 7 days. Of the 230 patients finally included (56.5% of the total), 112 (48.7%) received oral antibiotics (OST group) and 118 (51.3%) received IVT exclusively (IVT group). There was no significant difference in the total duration of antibiotherapy: OST 16 days (IQR, 14–21) vs. IVT 16 days (IQR, 13–21), p 0.591. Fig. 1 shows the patient's flowchart. Patients in OST had lower days of hospital stays from BC extraction to discharge (median 10 days (IQR, 6–15) vs. 17 days (IQR, 10–27), p < 0.001).

Cohort description

Table 1 shows the baseline and clinical characteristics of the patients included. The OST and IVT groups were similar in age and gender. There was a lower prevalence of unknown and respiratory focus in OST: 20.6% (22/107) vs. 32.8% (38/116), p 0.049, and 7.5% (8/107) vs. 18.1% (21/116), p 0.027, respectively, with no other differences in the primary focus or acquisition of bacteraemia. Patients receiving IVT had higher initial severity according to the SOFA score (3 points [IQR, 1–4] vs. 1 [IQR, 0–2], p < 0.001). Echocardiography was performed in 67.8% (154/227), with no difference between the groups (64.3% [72/112] vs. 71.3% [82/115], p 0.320). Source control was required in 50.9% (113/230) of patients, with no differences between the groups (53.6% (59/112) vs. 48.2% (54/118), p 0.425). Source control included catheter removal in 40.8% (89/230), surgery in 8.0% (18/230), and radiologist drainage in 3.1% (7/230).

Oral sequential therapy

Within the OST group, the switch to the oral route was made after 7 days (IQR, 4–11) of intravenous treatment, receiving 9 days (IQR, 7–14) of subsequent oral treatment (Fig. S1). 91.0% (102/112) received monotherapy. Patients were treated with amoxicillin/clavulanate (36.6%, 41/112), fluoroquinolones (31.2%, 35/112), and cephalosporins (16.1%, 18/112). Moreover, 52.7% (59/112) of patients received β-lactams. Table S1 summarizes the oral treatment options employed.

Table 2 describes the clinical outcomes. The primary endpoint occurred in 10.7% (11/112) in OST vs. 30.5% (36/118) in IVT

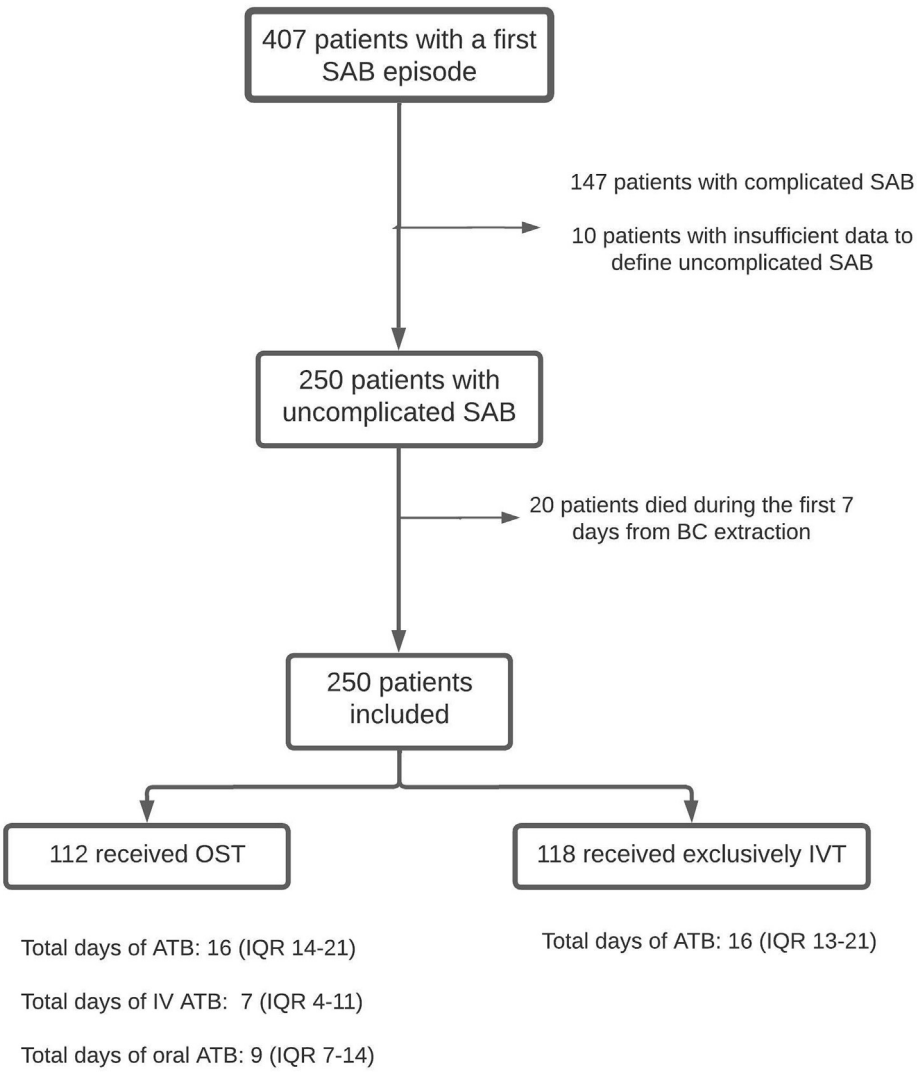

Fig. 1. Patients' flow chart. SAB: *Staphylococcus aureus* bacteraemia. BC, blood cultures; OST, oral sequential therapy; IVT, intravenous antibiotic therapy; ATB, antibiotic; IQR, interquartile range.

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Table 1
Baseline and clinical characteristics between groups. Continuous variables are expressed as median (interquartile range)

Variable		OST ($N = 112$)	IVT ($N = 118$)	p
Demographic and comorbidities				
Age (y)		68 (52–80)	68 (58–81)	0.525
Gender (female)		34.8% (39)	30.5% (36)	0.574
Charlson index		2 (0–4) (111/112)	2 (1–5)	0.599
Arterial hypertension		42.0% (47)	61.0% (72)	0.005
Diabetes mellitus		22.3% (25)	32.2% (38)	0.105
Chronic cardiac failure		19.6% (22)	33.9% (40)	0.017
Ischemic cardiopathy		13.4% (15)	23.7% (28)	0.062
Natural valvular disease		10.7% (12)	16.9% (20)	0.187
Chronic renal failure		15.2% (17)	23.7% (28)	0.134
Renal replacement therapy		4.5% (5)	6.8% (8)	0.310
Liver cirrhosis		2.7% (3/111)	2.5% (3)	1.000
Solid organ malignancy		27.0% (30/111)	18.6% (22)	0.156
Clinical presentation				
Acquisition	Community	28.6% (32)	29.7% (35)	0.472
	Nosocomial	50.9% (57)	55.9% (66)	
	HA	20.5% (23)	14.4% (17)	
Primary focus	Unknown	20.6% (22/107)	32.8% (38/116)	0.049
	Central catheter	13.1% (14/107)	9.4% (11/116)	0.526
	Peripheral catheter	25.2% (27/107)	21.5% (25/116)	0.527
	SSTIs	21.5% (23/107)	14.6% (17/116)	0.222
	Respiratory	7.5% (8/107)	18.1% (21/116)	0.027
	Other	12.2% (13/107)	5.1% (6/116)	0.153
Fever		92.9% (104/112)	88.0% (103/117)	0.265
Fever during first 48 h		36.5% (38/104)	33.0% (34/103)	0.662
Septic shock		14.3% (16)	28.2% (33/117)	0.015
SOFA score		1 (0–2) (111/112)	3 (1–4)	<0.001
Acute renal failure		28.4% (31/109)	36.8% (43/117)	0.203
Acute cardiac failure		9.0% (10/111)	18.8% (22/117)	0.037
Microbiology and management				
Methicilin-resistant SA		12.5% (14)	24.6% (29)	0.027
Vancomycin MIC >1,5		10.7% (12)	14.4% (17)	0.433
Time to positivity (h)		13 (10–17)	13 (10–16)	0.667
Positive control BC during first 48 h		18.3% (15/96)	20.8% (20/82)	0.709
Echocardiography (any)		64.3% (72/112)	71.3% (82/115)	0.320
Transoesophageal echocardiography		22.3% (25/112)	21.7% (25/115)	1.000
Source control procedures		53.6% (59)	48.2% (54)	0.425

Categorical variables are expressed as percentage (absolute number). Whenever the percentage or continuous measure does not address all patients in the group, the denominator is added. BC,____; IVT, Intravenous antibiotic therapy; OST, oral sequential therapy; SOFA, Sequential Organ Failure Assesment; HA, healthcare associated; SSTIs, skin and soft tissue infections.

($p < 0.001$). All-cause 90-day mortality was 6.3% (7/112) in OST vs. 28.0% (33/118) in IVT ($p < 0.001$). None of the deaths in OST were due to SAB or its complications (five cancer progression, one cardiac failure, and one pneumonia with negative BCs and no SA isolation) vs. 12 of 33 in IVT. SAB relapses occurred in 3.6% (4/112) in OST vs. 1.7% (2/118) in IVT (p 0.436). One patient in OST presented microbiological failure with no relapse (vertebral osteomyelitis).

Propensity-score matching and outcomes

PS matching was performed according to the methods previously described. The PSc consisted of 77 patients from each group. Table 3 shows the baseline and clinical characteristics in both groups within the PSc. Differences were correctly balanced, except for respiratory focus (6.9% (4/77) OST vs. 24.6% (14/77) IVT, p 0.022).

Table 2
Clinical outcomes in patients receiving oral antibiotics

Variable	OST ($N = 112$)	IVT ($N = 118$)	p1	β-Lactam ($N = 59$)	Non–β-lactam ($N = 53$)	p2
Primary outcome						
Composite 90-d endpoint	10.7% (12)	30.5% (36)	<0.001	8.5% (5)	13.2% (7)	0.544
Secondary outcome						
30-d mortality	0	22.0% (26)	<0.001	0	0	—
90-d mortality	6.3% (7)	28.0% (33)	<0.001	5.1% (3)	7.5% (4)	0.706
SAB-related 90-d mortality	0	10.2% (12/118)	0.001	0	0	—
90-d relapse	3.6% (4)	1.7% (2)	0.436	3.4% (2)	3.8% (2)	1.000
All-cause 90-d hospital readmission	18.8% (21)	15.3% (18)	0.489	15.3% (9)	22.6% (12)	0.342
Staphylococcus aureus bacteraemia-related 90-d hospital readmission	4.5% (5)	2.5% (3)	0.494	3.4% (2)	5.7% (3)	0.666
Serious adverse event leading to hospital readmission	0	0	—	0	0	—
Serious adverse event leading to antibiotic discontinuation	0	0	—	0	0	—

p1: univariate analysis comparing OST with IVT. p2: univariate analysis comparing β-lactam use with other antibiotics.

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Table 3
Baseline and clinical characteristics between groups in the propensity score-matched cohort

Variable		OST ($N = 77$)	IVT ($N = 77$)	p
Demographic and comorbidities				
Age (y)		69 (53-80)	67 (57-78)	0.665
Gender (female)		31.2% (24)	28.6% (22)	0.860
Charlson index		2 (0-4) (76/77)	2 (0-4)	0.605
Arterial hypertension		49.4% (38)	53.2% (41)	0.747
Diabetes mellitus		24.7% (19)	24.7% (19)	1.000
Chronic cardiac failure		24.7% (19)	24.7% (19)	1.000
Ischemic cardiopathy		14.3% (11)	22.1% (17)	0.296
Natural valvular disease		14.3% (11)	15.6% (12)	1.000
Chronic renal failure		14.3% (11)	22.1% (17)	0.296
Renal replacement therapy		5.2% (4)	6.5% (5)	0.719
Liver cirrhosis		3.9% (3)	2.6% (2)	0.681
Solid organ malignancy		19.7% (15/76)	19.5% (15)	1.000
Immunosuppression		14.3% (11)	13.0% (10)	1.000
Vascular lines in the previous 3 mo				
Peripheral venous catheter		66.2% (51)	67.5% (52)	1.000
Short term central catheter		11.7% (9)	15.6% (12)	0.639
Long term central catheter		9.1% (7)	9.1% (7)	1.000
Clinical presentation				
Acquisition	Community	27.3% (21)	31.2% (24)	0.712
	Nosocomial	51.9% (40)	53.2% (41)	
	HA	20.8% (16)	15.6% (12)	
Primary focus	Unknown	26.0% (20)	28.6% (22)	0.857
	Central catheter	14.3% (11)	11.7% (9)	0.811
	Peripheral catheter	22.1% (17)	24.6% (19)	0.849
	SSTIs	23.4% (18)	15.6% (12)	0.309
	Respiratory	6.9% (4)	24.6% (14)	0.022
	Genitourinary	6.5% (5)	2.6% (2)	0.442
	Others	3.9% (3)	1.3% (1)	0.620
Septic shock		16.9% (13)	19.5% (15)	0.835
SOFA score		1 (0–3)	2 (0–3)	0.507
Acute renal failure		37.7% (29)	29.9% (23)	0.394
Acute cardiac failure		11.7% (9)	11.7% (9)	1.000
Microbiology				
Methicillin-resistant *Staphylococcus aureus*		15.6% (12)	13.0% (10)	0.818
Time to positivity (h)		13 (10–17)	12 (10–16)	0.417
Management before oral therapy				
Initial combination antibiotic		44.2% (34)	39.2% (29/74)	0.621
Initial appropriate antibiotic		86.5% (64/74)	82.9% (58/70)	0.645

Continuous variables are expressed as median (interquartile range). Categorical variables are expressed as percentage (absolute number). Whenever the percentage or continuous measure does not address all patients in the group, the denominator is added. IVT, Intravenous antibiotic therapy; OST, oral sequential therapy; SOFA, Sequential Organ Failure Assesment; HA, healthcare associated; SSTIs, skin and soft tissue infections.

In the PS-matched cohort, during follow-up, 20.8% (32/154) patients presented the primary composite outcome, including 16.9% (26/154) 90-day mortality, and 4.5% (7/154) 90-day microbiological failures. Microbiological failures were mainly SAB relapses (3.9%, 6/154). Table 4 shows the analysis of primary and secondary endpoints in PSc. The primary composite endpoint was not more frequent in the OST group (relative risk, 0.42; 95% CI, 0.22–0.79). 90-day relapses occurred similarly in both groups (relative risk, 1.35; 95% CI, 0.75–2.39). Fig. S2 shows survival curves of primary and secondary endpoints according to treatment group. No adverse effects requiring suspension or change in antibiotherapy were detected in any patient. None of the readmissions were due to antibiotherapy side effects.

Discussion

Our main finding is that, in patients with uncomplicated SAB, OST was effective and safe. No deaths in the OST group were due to SAB or relapse of the bacteraemia. It was not associated with a higher risk of relapses, readmissions, or mortality than intravenous therapy. Importantly, in our study, 56.5% of patients with SAB met criteria for uncomplicated bacteraemia and would have been eligible for oral antibiotherapy.

Our results add to the limited body of literature supporting the use of oral antibiotherapy in these patients. To our knowledge, only one clinical trial has evaluated OST in patients with SAB [15]. However, a limited and heterogeneous number of patients were included (i.e. patients with or without bacteraemia, as well as patients with coagulase-negative staphylococcal bacteraemia), which limits its validity. Apart from this trial, few studies have evaluated oral treatment in uncomplicated SAB [16–18], and only one of them with a propensity-score matching method [16]. In our study, as in those aforementioned, switching to oral treatment after an initial period of intravenous treatment (5–7 days) was effective, with potential additional benefits in terms of costs and complications derived from prolonged hospital stays [19,20].

An interesting contribution of our work is the specific oral antibiotic used. Most patients received monotherapy, and half of the patients were treated with β-lactam antibiotics. Previous studies had proposed cotrimoxazole, clindamycin, or linezolid as the main oral alternatives [21,22]. Indeed, there is currently an ongoing clinical trial to evaluate the efficacy of sequential oral therapy with cotrimoxazole, clindamycin, or linezolid in these patients [23], without considering β-lactam antibiotics among the options. This proposal is due to their lower bioavailability [2,21,24]. Nevertheless, the former antibiotics can have important side effects when maintained longer >1 week [25], and β-lactams may be safer choices. Only a recent small retrospective cohort hypothesizes that step-down to oral antibiotic with β-lactams could be effective in uncomplicated SAB [17]. Studies on the use of oral β-

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Table 4
Primary and secondary endpoints in the propensity score-matched cohort

Variable	OST ($n = 77$)	IVT ($n = 77$)	p	RR (95% CI)
Primary endpoint				
Primary 90-d endpoint	10.4% (8)	32.5% (25)	0.001	0.42 (0.22–0.79)
Secondary endpoints				
30-d mortality	1.3% (1)	14.5% (11)	0.002	0.08 (0.01–0.62)
90-d mortality	3.8% (3)	29.8% (23)	<0.001	0.20 (0.08–0.58)
SAB-related 90-d mortality	0	9.1% (7)	0.014	Not calculable
90-d relapse	5.1% (4)	2.6% (2)	0.681	1.35, (0.75–2.39)
All-cause 90-d hospital readmission	20.8% (16)	19.5% (15)	1.000	1.04 (0.71–1.52)
SAB-related 90-d hospital readmission	6.4% (5)	3.9% (3)	0.719	1.27 (0.72–2.22)
Serious adverse event leading to hospital readmission	0	0	—	—
Serious adverse event leading to antibiotic discontinuation	0	0	—	—

IVT, Intravenous antibiotic therapy; OST, oral sequential therapy; RR, relative risk; SAB, *Staphylococcus aureus* bacteraemia.

lactams in the treatment of other bacteraemias have shown conflicting results [26,27]. Our results support that oral β-lactams in sequential oral therapy for uncomplicated SAB could be an option. However, these results must be interpreted with caution, as our study was underpowered to perform subgroup analysis, and we cannot extract any robust conclusion on the use of a specific antibiotic class in this setting.

Conversely, among the arguments against the use of oral antibiotics in these patients, we find a possible delay in the diagnosis of complicated SAB as well as the low number of patients meeting the strict low-risk criteria proposed by the authors of the aforementioned studies [16–18]. In these studies, <20% of the patients met the proposed low-risk criteria. However, it should be noted that these criteria lack validation. In contrast, patient selection in our study for uncomplicated SAB was based on a validated and widely used definition of the current international guidelines [3]. A recent survey study has shown a considerable agreement among infectious diseases experts in this definition [28]. In our study, more than half of our patients (56.7%) met the criteria for uncomplicated SAB and would have been eligible for OST, a similar proportion that what is described by other authors [16,29]. In a real-life scenario, including a low percentage of transoesophageal echocardiography [30], we found that the occurrence of complicated SAB, recurrence, or mortality in those managed with OST was low and similar to those managed with intravenous antibiotics exclusively. Hence, our data support the hypothesis that a significant percentage of patients with SAB (i.e. those who do not meet criteria for complicated SAB can be safely managed with oral antibiotherapy without increasing the risk of complicated SAB, relapse, readmission, or mortality). However, prospective randomized studies are needed to define which subgroups of patients with SAB can benefit from OST, as well as the most appropriate option of oral antibiotics.

Our study had certain limitations. First, the main one is that it is a single-centre study, with the inherent limitation of this type of design, especially selection bias (survivor). We have tried to minimize it by including patients who survived the first 7 days after index BC extraction. Second, patients receiving OST and IVT were not comparable. We have tried to minimize the differences between both groups by performing a well-balanced propensity-matched analysis. However, mortality in the OST group was still lower than that in IVT in the PSc, which was probably due to unmeasured confounding factors. In this regard, we could not retrieve information about the number of positive BC bottles, which has shown to be a prognosis factor [31]. Nevertheless, the comparison of clinical outcomes in our propensity-matched cohort confirms the safety of oral antibiotic step-down for these patients. Third, not all patients had control BC or echocardiographic assessment, which have been shown to influence patient prognosis [32]. Nevertheless, our study shows that, if the patient has evolved favourably, he/she can be transitioned to the oral route regardless of strict compliance with all management recommendations. This may facilitate that a larger number of patients with uncomplicated SAB in real life may be eligible for OST. Finally, the observational nature and relatively small sample size of our study make us cautious in drawing firm conclusions, especially subgroup comparisons between specific oral antibiotics (β-lactams vs. non–β-lactams). Prospective, randomized studies are needed to select which patients may benefit from OST and which particular oral antibiotic is most appropriate.

In conclusion, our data suggest that patients with uncomplicated SAB with good evolution after initial IVT can be rotated to oral antibiotic monotherapy. OST was not associated with higher hospital mortality, need for readmission or relapses than IVT exclusively, as well as could potentially save costs and complications of prolonged hospital stays. Prospective, randomized studies are needed to define which patients benefit from this type of management.

Author contributions

I.D.Y.: conceptualization, methodology, investigation, writing-original draft preparation. J.C.P.: conceptualization, methodology, software, investigation, formal analysis, data curation, writing-review and editing, supervision. A.M.V., J.M.V.C., B.S.A. investigation, and data curation. All other authors: writing- Review and editing.

Transparency declaration

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2023.02.001.

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