Antibacterial activity of recently approved antibiotics against methicillin-resistant Staphylococcus aureus (MRSA) strains: A systematic review and meta-analysis

Fei Liu¹, Sajad Rajabi², Chunhua Shi¹*, Ghazale Affirad³, Nazanin Omidi⁴, Ebrahim Kouhsari⁵,⁶, Saeed Khoshnood⁴ and Khalil Azizian⁷*

Abstract

Background: Methicillin-resistant Staphylococcus aureus (MRSA) infections are considered an important public health problem, and treatment options are limited. Accordingly, in this meta-analysis, we analyzed published studies to survey in vitro activity of recently approved antibiotics against MRSA isolates.

Methods: We searched electronic databases; PubMed, Scopus, and Web of Science to identify relevant studies (until November 30, 2020) that have focused on the in vitro activity of telavancin, dalbavancin, oritavancin, and tedizolid against MRSA isolates. Statistical analyses were conducted using STATA software (version 14.0).

Results: Thirty-eight studies were included in this meta-analysis. Overall in vitro activity of tedizolid on 12,204 MRSA isolates was 0.250 and 0.5 µg/mL for MIC₅₀ and MIC₉₀, (minimum inhibitory concentration at which 50% and 90% of isolates were inhibited, respectively), respectively. The overall antibacterial activity of dalbavancin on 28539 MRSA isolates was 0.060 and 0.120 µg/mL for MIC₅₀ and MIC₉₀, respectively. The overall antibacterial activity of oritavancin on 420 MRSA isolates was 0.045 and 0.120 µg/mL for MIC₅₀ and MIC₉₀, respectively. The overall antibacterial activity of telavancin on 7353 MRSA isolates was 0.032 and 0.060 µg/mL for MIC₅₀ and MIC₉₀, respectively. The pooled prevalence of tedizolid, telavancin, and dalbavancin susceptibility was 100% (95% CI: 100–100).

Conclusion: Telavancin, dalbavancin, oritavancin, and tedizolid had potent in vitro activity against MRSA isolates. The low MICs and high susceptibility rates of these antibiotics recommend a hopeful direction to introduce useful antibiotics in treating MRSA infections in the future.

Keywords: MRSA, Antibacterial activity, Tedizolid, Telavancin, Dalbavancin, Oritavancin, Lipoglycopeptide

Introduction

Staphylococcus aureus (S. aureus) is a prominent cause of hospital-acquired and community-acquired infections ranging from superficial skin and soft tissue infections to endocarditis [1, 2].

For two reasons, A) methicillin-resistant Staphylococcus aureus (MRSA) is a well-recognized public health problem worldwide [3], and B) Antibiotic-resistance pattern of MRSA. Currently, World Health Organization

*Correspondence: liufei126@163.com; k.azizian86@gmail.com
1 Department of Biomedical Engineering, Changzhi Medical College, Changzhi 046013, Shanxi, China
2 Department of Microbiology, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran
Full list of author information is available at the end of the article

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(WHO) considers *S. aureus*, especially MRSA, as one of the fundamental clinical challenges throughout the world. [4]. There are limited therapeutic options for the treatment of MRSA infections. Vancomycin is introduced as a drug of choice for treating serious infections due to MRSA. However, overuse of vancomycin leads to the emergence of non-susceptible strain [5–7]. For example, vancomycin-resistant *S. aureus* (VRSA) strains have been reported from many countries, including the USA, India, Iran, and Pakistan [5–7].

Furthermore, linezolid and clindamycin are other favorable antibiotics against MRSA infections [8]. Despite different mechanisms of action, the emergence of resistant strains to these antibiotics is rising [8–12]. Increased antibiotic resistance in MRSA isolates is one of this century’s most globally significant problems [4]. Several new agents such as telavancin, dalbavancin, oritavancin, and tedizolid have recently been licensed for the treatment of infections caused by MRSA.

Following the emergence of strains with reduced susceptibility to vancomycin (first generation of glycopeptide), the second generation of semisynthetic lipoglycopeptides has been developed as alternatives for treating MRSA infections. Telavancin, dalbavancin, and oritavancin have been introduced as critical lipoglycopeptide antibiotics recently approved by the Food and Drug Administration (FDA). Telavancin was the first approved lipoglycopeptide by the FDA in 2009 [13]. Furthermore, dalbavancin and oritavancin were first approved by the FDA in 2014 [14, 15]. Lipoglycopeptides are semisynthetic derivatives characterized by adding a lipophilic side chain, which prolongs their half-lives and increases their activities against Gram-positive cocci [16]. Lipoglycopeptides inhibit cell wall synthesis by binding to C-terminal D-alanyl-D-alanine (D-Ala-D-Ala) of cell wall precursor units [17, 18]. The N-alkyl-p-chlorophenylbenzyl substituent in oritavancin confers significantly enhanced activity against vancomycin-intermediate and resistant staphylococci [17]. In addition, lipoglycopeptides can interfere with cellular membrane functions [17, 19].

Linezolid, the first oxazolidinone antibacterial agent, was approved in the United States in early 2000. The following approved oxazolidinone was tedizolid. Tedizolid is a second-generation oxazolidinone class approved in 2014 by the FDA. This antibiotic is a bacteriostatic compound against gram-positive bacteria [20]. Similar to linezolid, the mechanical action of tedizolid is inhibiting protein synthesis by binding to the 23S ribosomal RNA of the 50S subunit [21]. Tedizolid is an oxazolidinone but differs from other oxazolidinones by possessing a modified side chain at the C-5 position of the oxazolidinone nucleus that improves potency through additional binding site interactions [22]. Not many in-depth studies are available that directly compare the susceptibilities of telavancin, dalbavancin, oritavancin, and tedizolid to different MRSA strains. Therefore, this systematic meta-analysis was conducted to survey in vitro activity of recently approved antibiotics against MRSA isolates by analyzing the related published studies.

Methods

Guidelines

This review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA) [23].

Search strategy

A systematic search was conducted to evaluate the antibacterial activity of recently approved antibiotics against MRSA strains. The electronic databases: Medline, Embase, and Web of Science were searched to identify relevant articles until November 30, 2020. The search strategy was based on keywords derived from our research questions. The keywords used in the search were: "tedizolid", "dalbavancin", "oritavancin", "telavancin", "delafloxacin", "Methicillin-Resistant Staphylococcus aureus", and "minimum inhibitory concentration". The Boolean operators were used to combine all descriptors. The search strategy was adapted to the features of each database. If possible, we searched for synonyms or used the search option for similar terms before every keyword. No limitation was applied during the searching procedure of databases, but the inclusion of the study in our full analysis required at least the English abstract to be available. The records found through database searching were merged, and the duplicates were removed using EndNote X7 (Thomson Reuters, New York, NY, USA). Reference lists of all eligible articles were also reviewed to find any additional potentially relevant studies. The flow chart of the selected articles is shown in Fig. 1.

Eligibility criteria

Identified studies that were consistent with the criteria included original articles published in English concerning the antibacterial activity of recently approved antibiotics against MRSA strains. After screening, duplicate studies, non-original articles (reviews, short communications, case studies, abstracts without full text, and book chapters), and studies that lack information regarding the minimum inhibitory concentration (MIC) were excluded. One reviewer performed the searches; then, initial screening was done by two independent reviewers for potentially relevant records matching the inclusion/exclusion criteria based on title and abstracts. Full articles were obtained from these records and were assessed...
Data extraction and quality assessment

Two reviewers coded and extracted the data independently. This process was also overseen by the third author again. All studies were consistent with the following inclusion criteria: (1) antibacterial activity was determined using one of the standard methods, including broth microdilution, agar dilution, and epsilometer (E)-test, (2) MIC50 and MIC90 (minimum inhibitory concentration at which 50% and 90% of isolates were inhibited, respectively) and their ranges were available, also (3) original studies that were performed on clinically derived isolates. Meanwhile, exclusion criteria were (1) studies that have not reported the MIC or have not used the standard susceptibility testing methods, (2) studies with a sample size < 10 isolates, and (3) studies performed on samples with animals or environment origin. Neither reviews nor systematic review articles, case reports, and articles available only in the abstract that lacks necessary information were included. Moreover, the quality of included studies was critically appraised using the Newcastle–Ottawa Scale [24]. The pre-defined review protocol was registered at the PROSPERO international prospective register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO, registration number CRD11111).

Statistical analysis

The meta-analysis was performed by computing the pooled using a random-effects model with Stata/SE software, v.17 (StataCorp, College Station, TX) on studies presenting raw data on antibacterial activity of tedizolid, dalbavancin, oritavancin, telavancin, and delafloxacin against MRSA strains. The inconsistency across studies was examined by the forest plot as well as the I² statistic. Values of I² (25%, 50%, 75%) were interpreted as the presence of low, medium, or high heterogeneity, respectively.
So, the DerSimonian and Laird random effects models were used [25]. Publication bias was assessed using Egger’s test. All statistical interpretations were reported on a 95% confidence interval (CI) basis.

**Study outcomes**

The primary outcome of interest was the pooled prevalence susceptibility of tedizolid, dalbavancin, and telavancin against MRSA isolates. The secondary outcomes of interest were the MIC$_{50}$ and MIC$_{90}$ of tedizolid, dalbavancin, and telavancin against MRSA isolates.

**Results**

**Systematic literature search**

A total of 540 records were identified in the initial search. Among these, 357 articles were excluded after an initial screening of the title and abstract due to their irrelevance and duplication. The full texts of the remaining 183 articles were reviewed (Fig. 1). Out of 183 articles, 145 were excluded for the following reasons: meta-analysis, review, conference abstract, and article without full text (n = 70), non-relevant data, or no MIC data (n = 75). Finally, the detailed characteristics of 38 included studies in this meta-analysis are indicated in Table 1.

**Characteristics of included studies**

All included studies had a cross-sectional design. All included studies in this meta-analysis were high-quality (Additional file 2: Table) [24]. However, most reports have been from America (n = 19), Asia (n = 8), Europe (n = 8), and multiple continents (n = 7). In the current study, to determine the effective concentration of tedizolid, dalbavancin, oritavancin, and telavancin against MRSA isolates, the mode of MIC$_{50}$, MIC$_{90}$, and MIC ranges was estimated (Table 2). To analyze the trends for changes in the tedizolid, dalbavancin, oritavancin, and telavancin susceptibility in recent years, we performed a subgroup analysis for two periods (2010–2015 and 2016–2020) (Tables 3, 5, Additional file 1: Figure). No significant difference was observed in the pooled prevalence of tedizolid, dalbavancin, oritavancin, and telavancin susceptibilities against MRSA isolate for two periods (2010–2015 and 2016–2020) (Tables 3, 4, 5).

**Antibacterial activity of tedizolid**

The prevalence of tedizolid susceptibility is available in 11 studies. The overall antibacterial activity of tedizolid was 0.060, and 0.120 µg/mL for MIC$_{50}$ and MIC$_{90}$ in 28539 MRSA isolates, respectively. Out of 11 studies, the pooled prevalence of dalbavancin susceptibility was 100% (95% CI: 100–100) (Table 6). There was no substantial heterogeneity among the 11 studies (p = 0.61; I$^2$ = 0%).

**Antibacterial activity of dalbavancin**

The prevalence of dalbavancin susceptibility is available in 8 studies. The overall antibacterial activity of dalbavancin was 0.032, and 0.060 µg/mL for MIC$_{50}$ and MIC$_{90}$ in 7353 MRSA isolates, respectively. From 8 studies, the pooled prevalence of telavancin susceptibility was 100% (95% CI: 100–100) (Table 6). There was no substantial heterogeneity among the eight studies (p = 0.86; I$^2$ = 0%).

**Antibacterial activity of oritavancin**

The prevalence of telavancin susceptibility was available in 2 studies. The overall antibacterial activity of oritavancin was 0.045, and 0.120 µg/mL for MIC$_{50}$ and MIC$_{90}$ in 420 MRSA isolates, respectively.

**Discussion**

MRSA is considered one of the most critical human health problems worldwide [26]. Empirical therapies by vancomycin and linezolid were reliable options for treating MRSA infections [27]. However, reports on decreasing susceptibility to vancomycin and linezolid are worrying [28]. It is critical to introduce and characterize new effective and safe antibiotics to prevent and control the infections related to MRSA strains [29]. The findings from a systematic review demonstrated that the prevalence of VRSA increased in recent years around the world [30]. It also was shown that different continents and countries are struggling with VRSA strains [30]. Compared with the classic glycopeptides, our meta-analysis shows a higher antibacterial activity of a new class of lipoglycopeptides (telavancin and dalbavancin susceptibilities were 100%). Moreover, the estimated MIC values of three lipoglycopeptides (MIC$_{50}$/MIC$_{90}$, 0.060/0.120 µg/mL for dalbavancin, MIC$_{50}$/MIC$_{90}$, 0.032/0.060 µg/mL for telavancin, MIC$_{50}$/MIC$_{90}$, 0.045/0.120 µg/mL for oritavancin) against MRSA strains are much lower than the MIC value of vancomycin for MRSA in the literature [31]. Moreover, against both vancomycin-resistant Enterococcus (VRE) and vancomycin-susceptible Enterococcus (VSE), the MIC value of lipoglycopeptides is much lower than the MIC value of vancomycin [16].
Table 1: The details included studies

| First author       | Study period | Publication year | Quality score | Continents/countries | Sample source          | No. MRSA isolates | Type of antibiotics | MIC50/MIC90 (µg/ml) | MIC range (µg/ml) | Susceptibility rate (%) | References |
|--------------------|--------------|------------------|---------------|----------------------|------------------------|------------------|---------------------|---------------------|-------------------|------------------------|------------|
| Gulseren Aktas     | 2005 and 2007| 2010             | 7             | Turkey               | clinical isolates      | 237              | Dalbavancin         | ≤0.008 / 0.25       | ≤0.008–2         | 99.6                   | [44]       |
| Gulseren Aktas     | 2014 and 2015| 2016             | 7             | Turkey               | clinical isolates      | 30               | Dalbavancin         | 0.12 / 0.12         | 0.03–0.12        | 100                    | [45]       |
| Maya Azrad         | 2015 and 2017| 2019             | 7             | Israel               | Blood sample, Wounds   | 275              | Tedizolid           | 0.25 / 0.3          | 0.19–0.5          | 100                    | [46]       |
|                    |              |                  |               |                      |                        | 275              | Dalbavancin         | MIC50: 0.047 / MIC90: 0.055 (wound)/0.06 (Blood sample) | 0.023–0.19 | 99.64                  | [46]       |
| Diane M. Citron    | No data      | 2014             | 6             | USA                  | osteomyelitis          | 15               | Dalbavancin         | 0.06 /0.06          | ≤0.03–0.12        | No data                  | [47]       |
| G. Ralph Corey     | 2011 to 2013 | 2016             | 7             | USA                  | blood culture and ABSSI | 405             | Orivancin           | 0.03 / 0.12         | 0.002–0.25        | 99.1                    | [48]       |
| Ko-Hung Chen       | 2013 to 2014 | 2015             | 7             | Taiwan               | ABSSI and pneumonia   | ABSSI (50) and pneumonia (50) | Tedizolid | ABSSI (0.25/0.25) and pneumonia (0.5/0.5) | ABSSI (0.25/0.05) and pneumonia (0.25/0.05) | 99.64 | [21] |
| Yong Pil Chong     | 2004 to 2009 | 2012             | 7             | Korea                | blood cultures         | 569              | Dalbavancin         | 0.25 / 0.25         | 0.06–0.25         | 98.8                    | [49]       |
| Aneta Guzek        | 2012 to 2014 | 2018             | 7             | Poland               | clinical isolates      | 124              | Dalbavancin         | 0.094/0.125         | 0.032–0.125       | 100                     | [50]       |
| Vanthida Huang     | No data      | 2010             | 7             | USA                  | clinical isolates      | 220              | CA-MRSA (110), MDR HA-MRSA (n = 110) | CA-MRSA: 0.0625/0.125, MDR HA-MRSA:0.125/0.125 | 0.015–0.006       | 100                     | [51]       |
| Ronald N. Jones    | 2011–2014    | 2017             | 7             | North American, Latin American, European, and Asia–Pacific Nations | bone and joint | 229              | Telavancin          | 0.03 / 0.06         | ≤0.015–0.006       | 100                     | [52]       |
| First author                     | Study period   | Publication year | Quality score | Continents/countries                                                                 | Sample source                                                                                       | No. MRSA isolates | Type of antibiotics                                                                 | MIC50/MIC90 (µg/ml) | MIC range (µg/ml) | Susceptibility rate (%) | References |
|---------------------------------|----------------|------------------|---------------|---------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|-------------------|-------------------------------------------------------------------------------------|---------------------|---------------------|------------------------|------------|
| James A. Karlowsky              | 2014 to 2016   | 2017             | 7             | Asia/Pacific region (Australia [n = 2], China [n = 16], New Zealand [n = 2], Philippines [n = 2], Taiwan [n = 2]), the Latin America region (Argentina [n = 2], Brazil [n = 10], Chile [n = 2], Colombia [n = 2], Mexico [n = 6]), Russia (n = 7), and Saudi Arabia (n = 1) | ABSSSI, blood samples, respiratory infections                                                                 | 1839              | Tedizolid                                                                           | 0.25 / 0.5          | 0.03–0.5            | 100                    | [53]        |
| Yangsoon Lee                    | 2011 to 2014   | 2015             | 7             | Korea                                                                                 | SSSIs, HAP                                                                                         | 1839              | Tedizolid                                                                           | 0.25 / 0.5          | 0.03–0.5            | 100                    | [54]        |
| María Carmen López-Díaz         | 2012 to 2014   | 2017             | 7             | Spain                                                                                 | clinical isolates                                                                                 | 1839              | Tedizolid                                                                           | 0.25 / 0.5          | 0.03–0.5            | 100                    | [55]        |
| Johanna Marcela Vane-gas Múnera | 2008 to 2010   | 2017             | 7             | Colombia                                                                              | clinical isolates                                                                                 | 1839              | Tedizolid                                                                           | 0.25 / 0.5          | 0.03–0.5            | 100                    | [56]        |
| Rodrigo E. Mendes               | 2011 to 2013   | 2015             | 7             | USA                                                                                  | clinical isolates                                                                                 | 1839              | Tedizolid                                                                           | 0.25 / 0.5          | 0.03–0.5            | 100                    | [57]        |
| Sandra P. McCurdy               | 2002–2012      | 2015             | 7             | USA, Europa, Russian and Israeli                                                      | clinical isolates                                                                                 | 1839              | Tedizolid                                                                           | 0.25 / 0.5          | 0.03–0.5            | 100                    | [58]        |
Table 1 (continued)

| First author                  | Study period   | Publication year | Quality score | Continents/countries                          | Sample source                          | No. MRSA isolates | Type of antibiotics | MIC50/MIC90 (µg/ml) | MIC range (µg/ml) | Susceptibility rate (%) | References |
|-------------------------------|----------------|------------------|---------------|-----------------------------------------------|----------------------------------------|-------------------|---------------------|---------------------|-------------------|--------------------------|-------------|
| R. E. Mendes                 | 2011–2014      | 2017             | 7             | North America (2150 isolates), Europe (1283), Latin America (473), and Asia-Pacific (APAC; 285) regions | blood samples                         | 1490              | Telavancin          | 0.03 / 0.06         | ≤0.015–0.12       | 100                      | [59]        |
| Jessica Baleiro Okado        | 2011-2012      | 2018             | 7             | Brazil                                       | clinical isolates                      | 27                | Tedizolid           | 0.25 / 0.25         | 0.125–0.5        | 100                      | [60]        |
| Michael A. Pfaffer           | 2014–2015      | 2019             | 7             | USA                                          | SSIs, bacteremia, pneumonia, intra-abdominal infections, urinary tract infections | 1732              | Tedizolid           | 0.12 / 0.12         | 0.03–0.25        | 100                      | [61]        |
| Philippe Proko-ciner         | 2008–2009      | 2012             | 7             | USA                                          | clinical isolates                      | 124               | Tedizolid           | 0.25 / 0.25         | 0.12–0.5         | 100                      | [62]        |
| Kenneth VI Rolston           | 2012–2013      | 2014             | 7             | USA                                          | clinical isolates                      | 50                | Telavancin          | 0.25 / 0.25         | 0.064–0.38        | No data                   | [63]        |
| Laser Sanal                  | 2013–2016      | 2018             | 7             | Turkey                                       | blood and tracheal aspirate            | 50                | Telavancin          | 0.032 / 0.064       | 0.016–0.125       | 100                      | [64]        |
| Suzannah M. Schmidt-Malän    | 1996–2014      | 2016             | 7             | USA                                          | clinical isolates                      | 35                | Tedizolid           | 0.5 / 0.5           | 0.25–0.5          | 100                      | [65]        |
| Wael Shams                   | 1991–2006      | 2010             | 7             | USA                                          | bloodstream, respiratory tract and wound | 168               | Telavancin          | 0.25 / 0.50         | 0.08–1.00         | No data                   | [66]        |
| Debora Sweeney               | 2017           |                  | 7             | USA                                          | clinical isolates                      | 15                | Oritavancin         | 0.06 / 0.12         | 0.03–0.12         | 100                      | [67]        |
|                              |                |                  |               |                                              | Dalbavancin                           |                   |                     |                     |                  |                          | [67]        |
|                              |                |                  |               |                                              | Telavancin                            | 0.06 / 0.06       | 0.03–0.12         | 100                      | [67]        |
|                              |                |                  |               |                                              | Telavancin                            | 0.06 / 0.06       | 0.06–0.12        | 100                      | [67]        |
|                              |                |                  |               |                                              | Telavancin                            | 0.25 / 0.5         | 0.25–0.5          | 100                      | [67]        |
| Jennifer I. Smart            | No data (2008) | 2016             | 7             | USA                                          | SSIs                                 | 700               | Telavancin          | 0.06/0.06           | 0.03–0.12         | 100                      | [68]        |
| Kenneth S. Thomson           | No data        | 2013             | 7             | USA                                          | clinical isolates                      | 111               | Tedizolid           | 0.5 / 0.5           | 0.12–0.5          | 100                      | [69]        |
| Floriana Campanile           | 2005–2007      | 2010             | 7             | Italia                                       | bloodstream, pneumonia, and SSIs       | 24                | Dalbavancin         | 0.06 / 0.12         | 0.03–0.12         | 100                      | [70]        |
Table 1 (continued)

| First author                  | Study period | Publication year | Quality score | Continents/countries                                                                 | Sample source                                                                 | No. MRSA isolates | Type of antibiotics | MIC50/MIC90 (µg/ml) | MIC range (µg/ml) | Susceptibility rate (%) | References |
|-------------------------------|--------------|------------------|--------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------|---------------------|---------------------|--------------------|----------------------------|------------|
| D. J. Biedenbach              | 2013–2014    | 2016             | 7            | Argentina, Brazil, Chile, Mexico, Australia and New Zealand, China                  | clinical isolates                                                            | Argentina, Brazil, Chile, and Mexico (318), Australia and New Zealand (51), China (425) | Tedizolid          | Argentina, Brazil, Chile and Mexico (0.5/0.5), Australia and New Zealand (0.25/0.5), China (0.25/0.5) | 0.12–0.5          | 100                         | ([39])                     |
| Carmen Betriu                 | 2004–2008    | 2010             | 7            | Spain                                                                               | Blood samples                                                              | 247               | Tedizolid           | 0.25/0.5            | 0.125–0.5         | 100                         | ([40])                     |
| Mekki Bensaci                 | 2009–2013    | 2017             | 7            | USA                                                                                 | clinical isolates                                                          | 3234              | Tedizolid           | 0.25/0.5            | 0.15 ≤ 0.015 to 2    | 99.6                        | ([71])                     |
| Hongbin Chen                 | 2009–2013    | 2014             | 7            | China                                                                               | SSSIs, lower respiratory tract infections                                   | 100               | Tedizolid           | 0.25/0.25           | 0.064–1            | No data                      | ([72])                     |
| Steven D. Brown              | No data      | 2010             | 7            | USA                                                                                 | clinical isolates                                                          | 129               | Tedizolid           | 0.5/1               | 0.12–16             | No data                      | ([73])                     |
| Jong Hwa Yum                  | 2002–2004    | 2010             | 7            | South Korea                                                                         | clinical isolates                                                          | 30                | Torezolid           | 0.5/0.5             | 0.5                 | 100                         | ([74])                     |
| Daniel F. Sahm               | 2011–2012    | 2015             | 7            | USA, Europe                                                                         | clinical isolates                                                          | 1770              | Torezolid           | 0.25/0.25           | 0.015–4             | 99.7                        | ([75])                     |
| Shuguang Li                   | 2014         | 2016             | 7            | China                                                                               | clinical isolates                                                          | 632               | Torezolid           | 0.25/0.25           | 0.064–0.5           | 100                         | ([76])                     |
| Marina Peñuelas              | No data      | 2016             | 7            | Spain                                                                               | clinical isolates                                                          | 18                | Torezolid           | 0.25/0.25           | 0.125–0.5           | 100                         | ([77])                     |
| Michael A. Pfaller           | 2014         | 2016             | 7            | Asia–Pacific, Eastern Europe, and Latin American Countries                         | clinical isolates                                                          | 701               | Tedizolid           | 0.12/0.12           | 0.03–0.25           | 100                         | ([78])                     |

ABSSSI acute bacterial skin and skin structure infections, CA-MRSA community-associated MRSA infections, HA-MRSA healthcare-acquired methicillin-resistant Staphylococcus aureus, HAP hospital-acquired pneumonia
MIC50/90 values of dalbavancin (0.06/0.12 µg/mL) are very similar to another systematic review published by Sadr in 2017 [32]. Moreover, compared to vancomycin, previous studies indicated that dalbavancin showed potent activity against biofilm-forming bacteria [33, 34]. However, a network meta-analysis showed no significant differences between dalbavancin and vancomycin in treating acute bacterial skin and soft-tissue infections (SSTIs) [35]. Dalbavancin susceptibility was more than 99% in the published systematic review in 2017, as our results [32].

In our study, the MIC50 value of oritavancin against MRSA strains is similar to a systematic review by Mendes et al. in 2015 [36]. Solo clinical trials show that oritavancin is more effective than vancomycin against MRSA infections [37]. Mendes et al. [36] evaluated the activity in vitro of oritavancin and comparators against Gram-positive pathogens causing SSTIs in European and US hospitals. They showed that oritavancin susceptibility in Gram-positive clinical isolates from the United States and Europe were 98.4% and 98.9%, respectively [36]. However, our meta-analysis studied worldwide data, and oritavancin susceptibility was 100%.

A previous systematic review and meta-analysis published in 2019 reported that the MIC50 and MIC90 of tedizolid were 0.250 and 0.500 µg/mL, respectively [38]. These MIC values are lower than the MIC values of vancomycin against MRSA strains [39, 40]. It was also shown that the MIC of tedizolid is much lower than the MIC of vancomycin against VISA strains [41]. In addition, tedizolid demonstrated greater in vitro potency than linezolid against MRSA strains, but further research is required for a treatment recommendation. However, published studies showed that some adverse events are related to the
simultaneous administration of telavancin and tedizolid [42, 43]. Moreover, in our meta-analysis, the MIC values and susceptibility rates for all four antibiotics were investigated in two periods (2010–2015 and 2016–2020), and findings were very similar between the two periods. The limited use of these antibiotics and their specific action mechanisms help explain this lack of change.

In conclusion, our results demonstrated that dalbavancin, oritavancin, telavancin, and tedizolid have antibacterial activity in vitro against MRSA isolates. However, future preclinical and clinical research are necessitated to support our findings.

Abbreviations
MRSA: Methicillin-resistant Staphylococcus aureus; MIC<sub>50</sub>: Minimum inhibitory concentration at which 50% of isolates were inhibited; MIC<sub>90</sub>: Minimum inhibitory concentration at which 90% of isolates were inhibited; S. aureus: Staphylococcus aureus; VRE: Vancomycin-resistant Enterococcus; SSTIs: Skin and soft-tissue infections.

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s12941-022-00529-z.

Additional file 1: The quality assessment of included studies in this meta-analysis.
Additional file 2: Antibacterial activity of dalbavancin telavancin, tedizolid, and dalbavancin against MRSA isolates based on year groups.

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Author contributions
FL, EK, GHA, SKh, and SR, NO contributed to the work’s conception, design, drafting, and extraction of data. Ch. Sh, Kh. A. Contributed to revising and final approval of the version to be published. All authors agreed and confirmed the manuscript for publication. All authors read and approved the final manuscript.

Author’s information
Khalil Azizian; Ph. D of Medical Bacteriology in Kurdistan University of Medical Sciences. His research interests are working on nosocomial infections. He has experience in diagnostics infections and antimicrobial resistance testing.

Table 6 The pooled prevalence susceptibility of tedizolid, oritavancin, dalbavancin, and telavancin against MRSA isolates

| Antibiotics      | Number of studies | Number of MRSA isolates | Proportion (95% CI) | chi²  | Heterogeneity P | I²     | p  |
|------------------|-------------------|-------------------------|---------------------|-------|-----------------|-------|----|
| Dalbavancin      | 11                | 28539                   | 1.00, (1.00,1.00)    | 8.22  | 0.61            | 0.00% | 0.00|
| Oritavancin      | 2                 | 420                     | 1.00, (1.00,1.00)    | 7.57  | 0.99            | 0.00% | 0.00|
| Tedizolid        | 21                | 12204                   | 1.00, (1.00,1.00)    | 3.26  | 0.86            | 0.00% | 0.00|
| Telavancin       | 8                 | 7353                    | 1.00, (1.00,1.00)    |       |                 |       |    |

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Availability of data and materials
All the data in this review are included in the manuscript.

Declarations
Ethical approval and consent to participate
The study protocol was approved by the Health Research Ethics Committee of the Golestan University of Medical Sciences (reference no. IR.GOUMS.REC.1401.139).

Consent for publications
Not applicable in this section.

Competing interests
The authors declare that they have no competing interests.

Author details
1 Department of Biomedical Engineering, Changzhi Medical College, Changzhi 046013, Shanxi, China. 2International Medical Campus, Iran University of Medical Sciences, Tehran, Iran. 3Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. 4Clinical Microbiology Research Center, Ilam University of Medical Sciences, Ilam, Iran. 5Laboratory Sciences Research Center, Golestan University of Medical Sciences, Gorgan, Iran. 6Department of Laboratory Sciences, Faculty of Paramedicine, Golestan University of Medical Sciences, Gorgan, Iran. 7Department of Microbiology, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran.

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