SP 54: What are the preferred antibiotics for empirical antibiotic therapy in pyogenic spinal infections?

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Response/Recommendation : Based on the available data, the authors consider that the choice of empirical antibiotic therapy (EAT) should be considered based on the host, the clinical situation, and the epidemiologic risk, as well as the local historical in vitro susceptibility data of the expected pathogen. Although, first generation cephalosporins are generally recommended against Staph. Aureus as first line, a combination of rifampicin with fluoroquinolones may be considered in areas with low incidence of resistance after excluding Mycobacterium tuberculosis. Vancomycin may be combined when resistant strains of gram positive cocci are considered. Broad-spectrum cephalosporin or carbapenem may be an alternative for fluoroquinolone when resistant strains of gram negative rods are expected.

Level of Evidence: Low

Delegate Vote:

Rationale:

A systematic review was conducted to analyze the preferred antibiotics for empirical therapy in pyogenic spinal infections (PSI). PubMed, Web of Science, Clinicaltrials.org and Scopus were searched from inception till December 01, 2024, for original articles reporting antibiotic usage for empirical therapy in PSI. We excluded published in non-English language, case reports, review articles, registry-based studies, studies with only paediatric population, and studies on tubercular spondylodiscitis. We also excluded studies that did not describe the standardized empirical antibiotic therapy (EAT) protocol employed in the patients along with their susceptibility profile. We conducted the systematic review in strict adherence to the guidelines of the Cochrane Handbook of Systematic Reviews for Interventions (1). Initial database screening resulted in 488 articles which after duplicate removal resulted in 362 articles that were subjected to tile and abstract screening. We shortlisted 22 articles for full-text screening from the 362 articles and included 7 articles(2–8) in the review that met the inclusion criteria. All the studies were of retrospective nature and provided level IV evidence.

Despite the increased availability of recent diagnostic methods, the causative organisms in all PSI could not be identified and there is a need to start the patients on EAT (9). WHO has emphasized the rational antibiotic usage that is appropriate for the clinical condition for an adequate period that meets the clinical needs at a low cost to the patient and their community (10). However, there is no clear consensus on the right choice of EAT for PSI. The included studies were published between 2008 – 2022 including 904 patients with PSI who received EAT in their management. The EAT regimen and its susceptibility to the underlying organisms noted in the studies are listed in **Table 1**. We noted variation in the EAT in the included studies to range from 6 – 15.1 weeks.

Pola et al.(11) evaluated the studies on PSI for 20 years and suggested the EAT be prescribed during the waiting period for culture reports and in culture-negative individuals. The choice of antibiotics used in the EAT depends on the factors such as bone and disc penetration capability, potential side effects, and administration feasibility. They recommended that the EAT to consist of broad-spectrum agents covering *Staphylococcus aureus* since they are the most common organisms involved in PSI. Further, consideration should be given to the clinically suspected organisms. Although no high-quality data on the optimal treatment duration, the recommended duration of the treatment range from 4-12 weeks as noted in the included studies. Suggested markers to consider antibiotic discontinuation in the included studies are normalization of the inflammatory markers such as ESR and/or CRP, reduction of spinal pain, normalization of body temperature and improvement in plain radiography.

Although an early switch to oral antibiotics is not recommended, with the availability of oral agents with higher bioavailability and bone penetration such as clindamycin and fluoroquinolones, early oral administration could be considered (12,13). . Further, Infectious Diseases Society of America in their antibiotic selection guidelines also recommended carbapenams for combination with vancomycin in such resistant scenarios (14).

Table 1: Characteristics of studies included in the analysis.

Sl. No	Author	Year	Sample size	Empirical Antibiotic Therapy	Susceptibility	Treatment duration
1	P Viale et. al	2008	48	Levofloxacin + Rifampicin	84.1%	15.1 weeks
2	J Lora-Tamayo et al.	2011	72	Levofloxacin + Rifampicin	93%	8 weeks
3	S Desoutter et al.	2015	101	Ofloxacin + Rifampicin	58%	6-12 weeks
				Levofloxacin + Rifampicin	75%	
				Ciprofloxacin + Clindamycin	76%	
				Ciprofloxacin + Amox/Clav	77%	
4	J Urrutia et al.	2015	97	Ciprofloxacin + Cephalosporins	Not reported	12 weeks
5	G Mohamad et al.	2018	45	Ciprofloxacin + Cephalosporins	Not reported	12 weeks
6	KH Park et al.	2019	358	Levofloxacin + Rifampicin	73.5%	>8 weeks
				Levofloxacin + Clindamycin	71.2%	
				Ciprofloxacin + Amox/Clav	64.5%	
				Vancomycin + Ciprofloxacin	93%	
				Vancomycin + Ceftriaxone	94.1%	
				Vancomycin + Ceftazidime	95.8%	
				Vancomycin + Cefepime	95.8%	
7	SH Lee et al.	2022	183	Cephalosporins	89%	6 weeks

Among the included studies, levofloxacin with rifampicin is the most commonly preferred regimen of choice considering its penetration capability and oral administration feasibility with considerable susceptibility ranging from 73.5%-93% (3–5). Urrutia et al.(8) and G Mohamad et

al.(6) noted the combination of Ciprofloxacin and Cephalosporins resulted in a cure of the disease without any relapse. In scenarios where resistance strains such as methicillin-resistant *Staph. aureus* is suspected, Park et al.(4) noted vancomycin with cephalosporins such as Ceftazidime/Cefepime resulted in a significantly better susceptibility profile (95.8%) compared to the other combinations such as levofloxacin with rifampicin (73.5%) discussed above.
EAT is dependent on the host, the clinical situation, and the epidemiologic risk, as well as the local historical in vitro susceptibility data. Hence, a two-tiered approach is suggested in the choice of antibiotic regimen. First, rifampicin with fluoroquinolones could be considered in areas with low incidence of resistant strains of *Staph. aureus* after excluding *Mycobacterium tuberculosis* (15,16). If healthcare-associated resistant strains are expected, vancomycin combined with broad-spectrum cephalosporin or fluoroquinolone or carbapenams could be considered as the EAT for PSI (4,16).

Our study has potential limitations. We noted significant heterogeneity in the duration of antibiotic protocols utilized in the included studies and their follow-up periods. Although all the cases in the included studies were of non-tuberculous PSI, two of the included studies involved only culture-negative patients, hence the susceptibility profile of their antibiotic regimen could not be assessed appropriately although the outcome of the patients was reported. Further, the dosage of the included antibiotic regimens was heterogeneous across the included studies which prevented further quantitative analysis of the reported results.

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