INFLUENCE OF PERIOPERATIVE ANTIBIOTIC PROPHYLAXIS ON TIME TO POSITIVITY AND PROPORTION OF POSITIVE SAMPLES: A COHORT STUDY OF 60 CUTIBACTERIUM ACNES BONE AND JOINT INFECTIONS.

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ABSTRACT

Background
Cases of suspected bone or joint infections require intraoperative microbiological testing before antibiotic treatment. This theory implies that perioperative antibiotics may induce poor culture findings, hindering personalized antibiotic therapy. In *Cutibacterium acnes* infections of bone and joints, antibiotic prophylaxis 30–60 minutes before surgery affected the duration and proportion of positive microbiological samples. Determining how perioperative antibiotic prophylaxis affects *Cutibacterium acnes* bone and joint infection microbiological sample positive time and proportion.

Methods
A retrospective analysis was conducted including patients with at least one *Cutibacterium acnes*-positive sample within a year. Patients were classified as exhibiting an "infection" if a minimum of two samples yielded positive results. Conversely, patients were deemed to have experienced sample "contamination" if less than two samples yielded positive results. The utilization of Kaplan-Meier curves was employed in order to visually represent the duration of time required for cultures to yield positive test results.

Results
The cases included 60 *C. acnes* infections and 44 contaminations. Compared to 54.8% in the contamination cohort, 71.8% in the infection cohort utilized perioperative prophylaxis. In the cohort of infected individuals, the mean time to positive results was 7.06 days for perioperative prophylaxis and 7.09 days for patients without it. Sample positivity did not affect perioperative prophylactic usage, which was 70.6% and 64.9%.

Conclusion
The administration of perioperative prophylaxis did not exhibit any deleterious impact on the microbiological yield observed in *C. acnes* infections. Henceforth, the implementation of regular antibiotic prophylaxis is deemed a safe and effective measure in the prevention of surgical site infections.

Recommendation
It appears that perioperative preventative antibiotics for bone and joint *Cutibacterium acnes* infections are safe and effective. Continue antibiotic prophylaxis to prevent surgery site infections without compromising microbiological samples. Further study can establish when to provide antibiotics to improve efficacy and diagnosis.

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INTRODUCTION
Orthopedic surgeons routinely provide antimicrobial prophylaxis to prevent surgical site infection and orthopedic device colonization [1]. An antibiotic with bactericidal characteristics should be given thirty to sixty minutes before skin incision surgery. *Staphylococci, Streptococci,* and *Cutibacteria* are targeted and eliminated in this procedure.

Despite antibiotic treatment, orthopedic bone and joint infections occur at 1–10% [2]. Biofilms breed germs that cause orthopedic bone and joint diseases. Biofilm

distribution is heterogeneous, making infection localization difficult for diagnostic sampling. Metabolic inertia and non-replication make biofilm bacteria impervious to drugs and the immune system. Biofilm bacteria are protected from antimicrobials and immunological reactions by a polymeric matrix. Thus, biofilm bacterium retrieval, isolation, and culturing are difficult [3]. Biofilm infections, especially bone and joint infections, are difficult to diagnose due to many causes. Due to these challenges, perioperative antibiotic prophylaxis is often avoided when a bone or joint infection is suspected and surgical intervention is needed to improve intraoperative biopsy cultures for pathogen identification [4]. To create a customized long-term antimicrobial treatment, the causal bacterium must be identified.

Recent studies [5, 6] have shown that perioperative single-shot prophylaxis with antibiotics before intraoperative microbiological collection does not increase culture-negative outcomes. In septic orthopedic surgeries, perioperative antibiotic treatment has been shown to significantly reduce infection rates. However, the above studies had small sample numbers, limiting their generalizability. The diseases' heterogeneity, including highly virulent and less virulent organisms, is also concerning.

The observed growth rate is characterized by a slow progression. *C. acnes*, a Gram-positive anaerobic bacterium, has been identified as a causative agent in the development of bone and joint infections. Hence, the investigation of perioperative antibiotic prophylaxis in the field of orthopedics holds significant utility [7]. Prior investigations have predominantly focused on the impact of perioperative prophylaxis on intraoperative culture outcomes. Nevertheless, limited research has been conducted to investigate the quantification and ratio of affirmative specimens, as well as the duration required for the identification or validation of infection.

This investigation expands on previous findings from a large and homogenous cohort of people with suspected *C. acnes* bone and joint infections. Perioperative antibiotic prophylaxis was examined to determine how long *C. acnes* samples take to test positive. This metric is crucial for doctors when planning treatment. Additionally, the number of positive samples and duration needed to confirm *C. acnes* infections in patients who received perioperative antibiotic prophylaxis were compared to those who did not.

METHODS

Study design

A retrospective study was conducted.

Study setting

The study was conducted at the Anugrah Narayan Magadh Medical College, Gaya, India, from a duration of November 2021 to October 2022.

Inclusion criteria

encompassed patients who exhibited a minimum of one positive intraoperative sample for *Cutibacterium acnes* within one year.

Exclusion criteria

encompassed patients lacking accessible data pertaining to antibiotic prophylaxis, as well as those who had undergone antibiotic treatment for a duration exceeding 24 hours within a 14-day period preceding the collection of samples.

Study size

To arrive at the final sample size of 100 participants, inclusion and exclusion criteria were established. This stringent selection process, along with the integration of cases with more than three analyzable samples to ensure accurate classification, ultimately resulted in a total of 100 participants for the study.

Bias

There was a chance that bias would arise when the study first started, but we avoided it by giving all participants the identical information and hiding the group allocation from the nurses who collected the data.

Data Collection

The clinical and demographic data were extracted from the individual's clinical records of the orthopedic center and the infectious diseases consultation service. Microbiological data were obtained and documented from the Anugrah Narayan Magadh Medical College, Gaya.

Grouping of Patients

The patients were stratified into two discrete cohorts: the "infection" cohort, encompassing individuals in whom *C. acnes* was identified in at least two separate samples within the same individuals case, and the "contamination" cohort, comprising people who had only one positive sample for *C. acnes*. For the purpose of achieving accurate classification, the inclusion of cases encompassing more than three analyzable samples was integrated.

Statistical Analysis

The data regarding the diagnostic modality utilized for the detection of *C. acnes* in each specimen was collected. The determination of the time to positivity of *C. acnes* growth

involved the calculation of the duration in days from the commencement of microbiological culture to the identification of *C. acnes*. The present analysis was primarily concerned with ascertaining the proportion of microbiological samples that exhibited positive outcomes. Sensitivity analyses were performed to account for potential discrepancies in the quantity of samples obtained from individual patients. Statistical analyses were conducted using Stata 15.0 SE software.

Microbiological Processing

Diagnostic cultures encompassed a multitude of procedural steps, including the aforementioned incubation process, as delineated earlier. The determination of the time to positivity of *C. acnes* growth was conducted utilizing specific criteria, including the assessment of colony formation and turbidity in the culture media.

RESULTS

Clinical Data and Antibiotic Prophylaxis

A cohort of 100 individuals was subjected to examination, predominantly comprising males (68.1%), with a median age of 57.5 years. These participants collectively provided a sum of 500 intraoperative samples within the specified 'time period'. The shoulder (n = 71) and hip (n = 24) were identified as prevalent sample sites. In a majority of patients (86.3%), the presence of a prosthesis or foreign body was observed. A diagnosis of *C. acnes* infection was established in 60 patients (57.2%) based on the presence of at least two positive samples. Conversely, 44 patients (40.8%) exhibited only one positive sample, which was deemed as indicative of sample contamination. Out of the total of 500 samples collected, the majority (87%) consisted of tissue biopsy specimens, followed by sonication fluid from removed implants (8.8%), and bone biopsy specimens (1.2%). In the infection group, the mean number of samples per patient was determined to be 4.3, while in the contamination group, it was found to be 3.5. Among the cohort of 60 patients in the infection group, a notable proportion of 67.8% were found to have not undergone perioperative prophylaxis prior to the collection of samples. In contrast, within the contamination group, the corresponding percentage was observed to be 50%. Cefuroxime was observed to be the predominant antibiotic prophylaxis, accounting for 82.7% of the total usage.

Table 1: Clinical characteristics

Clinical characteristics	No. of patients		
	Overall (%)	With infection (%)	With no infection (%)
Patient characteristics			
Male	75	44	31
Age	57.5	57.5	57.5
Sample size			
Shoulder	71	46	25
Hip	24	11	13
Spine	4	3	1
Knee	5	1	4
Other	2	0	2
Sample type			
Tissue and/or bone	78	48	30
Sonication fluid	29	15	14
Mean no. of positive samples per case [IQR]	2	2	0
Presence of foreign body			
Prosthesis	57	30	27
Other foreign body	37	27	10
Perioperative prophylaxis, yes	42	20	22
Prophylaxis agent			
Cefuroxime	34	16	18
Cefazolin	4	2	2
Clindamycin	2	0	2
Vancomycin	1	1	0

Time to Sample Positivity

Corynebacterium acnes was identified in 47.8% of the samples. The duration required for the culture to yield positive results was notably shorter in the infection group (5.04 days) as opposed to the contamination group (7.37 days). Upon examination of the infection cohort, it was observed that the duration until the manifestation of positive results did not exhibit any substantial variation between specimens obtained from individuals who received perioperative prophylaxis and those who did not.

Proportion of Sample Positivity

In the present study, it was observed that approximately 49.9% of the patients included in the sample exhibited positive test results. There was an absence of a statistically significant disparity in sample positivity rates observed between patients who received perioperative prophylaxis and those who did not. Within the cohort of patients afflicted with infection, no statistically significant discrepancy was noted in the rate of sample positivity between individuals who underwent perioperative prophylaxis and those whose did not.

DISCUSSION

The present study sought to investigate the impact of preoperative administration of antibiotics on the duration of diagnosis and rates of positive sample identification in cases of bone and joint infections attributed to *C. acnes*. The aforementioned infections represent a significant health concern and can incur substantial financial burden in terms of treatment expenses [8]. The prompt recognition of a condition is imperative for the implementation of optimal therapeutic interventions [9]. The present study revealed that the administration of antibiotics prior to surgical procedures did not result in any significant delay in the diagnosis of *C. acnes* infections. This finding provides further support for the regular utilization of these antibiotics, as previous research has demonstrated their efficacy in reducing infection rates. In the context of hip and knee surgeries, the implementation of appropriate antibiotic administration has demonstrated a significant decrease in the incidence of wound infections [10].

The prevalence of positive samples within the study cohort exhibiting *C. acnes* infections demonstrated no significant disparity between patients who underwent antibiotic treatment prior to surgery and those who did not (64.9% vs. 67.8%). The aforementioned infections frequently entail the presence of protective biofilms, thereby conferring resistance against a multitude of antibiotics [9, 11]. Preoperative administration of antibiotics primarily focuses on eradicating bacteria present in the bloodstream and tissues, while exerting minimal influence on biofilms. Consequently, the administration of antibiotics does not

significantly alter the outcomes of culture results obtained from samples collected during surgical procedures [12].

It is strongly advised to employ a regular administration of antibiotics prior to surgical procedures, even in cases where there is suspicion of a *C. acnes* infection, as it has been observed that such administration does not have an impact on the diagnostic efficacy of the surgical intervention. This observation is consistent with the recommendations put forth by the American Academy of Orthopedic Surgeons [13] and a recent systematic review [14], both of which have reported no statistically significant disparity in culture outcomes when comparing the administration of antibiotics prior to surgery versus no administration. The aforementioned recommendations are not encompassed within the guidelines established by the French regulatory authorities [15] or the Infectious Diseases Society of America (IDSA) guidelines published in 2013 [4].

The study's notable attribute resides in its substantial and uniform cohort comprising 60 cases, all of which have been definitively diagnosed with bone or joint infections caused by *C. acnes*. This cohort represents the most extensive investigation of its nature, specifically targeting this particular pathogen. A pathogen of reduced virulence was deliberately selected in order to provoke the diagnostic procedure. The present study encompasses an examination of the diagnostic duration and prevalence of positive samples across diverse cohorts of patients, thereby offering a unique vantage point. The implementation of the well-established microbiological protocols guarantees the attainment of dependable culture outcomes.

Generalizability

The findings from this study have broader implications for a larger population of patients undergoing surgical procedures, particularly in cases of bone and joint infections associated with *C. acnes*. These infections carry significant healthcare and financial burdens, underscoring the importance of timely diagnosis and effective treatment. The study's conclusion that preoperative antibiotic administration does not result in delays in diagnosis or significantly affect the rates of positive sample identification is reassuring. This supports the continued use of antibiotics before surgery, as it has been shown to reduce infection rates in various surgical contexts. Additionally, the study's observation that antibiotic administration does not substantially impact culture results aligns with recommendations from reputable organizations like the American Academy of Orthopedic Surgeons. The study's substantial and diverse cohort, comprising 60 definitively diagnosed cases, adds weight to its findings and offers valuable insights into diagnostic processes for this pathogen.

CONCLUSION

In summary, the study results indicate that preoperative administration of antibiotics in the context of elective orthopedic infection surgeries does not exert any discernible influence on the diagnostic yield of microbiological cultures. It is strongly advised to implement a regular administration of these antibiotics in order to mitigate the likelihood of surgical field infections and safeguard the integrity of recently implanted hardware.

Limitations
It is imperative to acknowledge that the study is constrained by its retrospective design, thereby influencing the accessibility of data and the ability to make comparisons with control groups.

Recommendation
Based on the findings, the practice of administering perioperative prophylactic antibiotics for *Cutibacterium acnes* infections affecting bone and joints appears to be safe and effective. It is advisable to continue the use of regular antibiotic prophylaxis to prevent surgical site infections without significant adverse effects on microbiological sample outcomes. Further research can explore optimal timing for antibiotic administration in such cases to maximize its efficacy while maintaining diagnostic accuracy.

Acknowledgment

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