



# Efficacy of Empirical Ampicillin Sulbactam + Clindamycin Treatment in Deep Neck Infections in Adults

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**Cite this article as:** Alagöz S, Delibaş V, Bal KK, Özdaş T, Erdoğan AM, Kütük SG, et al. Efficacy of empirical ampicillin sulbactam + clindamycin treatment in deep neck infections in adults. JEURMEDS 2021;2(3):75-79.

## ABSTRACT

**Objective:** Deep neck infection (DNI) is defined as an infection that occurs in the potential cavities and fascia of the neck. DNI is an Ear Nose Throat (ENT) emergency that needs to be treated early and effectively. It is important to preserve the airway patency, especially in the follow-up. DNI can be seen in all age groups, which are difficult to diagnose due to location differences and have a high risk of complications. Nowadays, odontogenic infections are the most common cause of infections in adults. To investigate the effectiveness of DNI empirical ampicillin sulbactam + clindamycin treatment in adults.

**Material and Methods:** The information of 36 patients who were hospitalized and treated with the diagnosis of deep neck infection between October 2017 and September 2020 was reached in University of Health Sciences: Adana City Training and Research Hospital ENT outpatient clinic.

**Results:** The ages of the patients were between 19 and 73, with a mean of  $41 \pm 14.433$ . As the age increased, the duration of treatment was prolonged. In empirical treatment, meropenem 1 (2.8%), ertapenem 1 (2.8%), ceftriaxone + metronidazole 6 (16.7%), ampicillin sulbactam + clindamycin 26 (72.2%), ampicillin sulbactam 2 (2%, 8) has been used in the patient. While 30 (83.3%) patients were drained, 6 (16.7%) patients were not drained. The most frequently affected area is the submandibular area. (47.2%).

**Conclusion:** We think that a successful response was obtained from empirical ampicillin sulbactam + clindamycin treatment.

**Keywords:** Neck, bacterial infections, abscess, anti-bacterial agents, adult

## ÖZ

### Erişkin Derin Boyun Enfeksiyonlarında Ampirik Ampisilin Sulbaktam + Klindamisin Tedavisinin Etkinliği

**Giriş:** Derin boyun enfeksiyonu (DBE), boyunun potansiyel boşluklarında ve fasyasında oluşan bir enfeksiyon olarak tanımlanır. DBE, erken ve etkili bir şekilde tedavi edilmesi gereken bir Kulak Burun Boğaz (KBB) acil durumudur. Özellikle takipte hava yolu açıklığının korunması önem arz eder. Lokasyon farklılıkları nedeniyle teşhisi zor, komplikasyon riski yüksek olan ve tüm yaş gruplarında görülebilen bir hastalıktır. Günümüzde odontojenik enfeksiyonlar, yetişkinlerde enfeksiyonların en yaygın nedenidir. Yetişkinlerde DBE ampirik ampisilin sulbaktam + klindamisin tedavisinin etkinliğini araştırmayı amaçladık.

**Gereç ve Yöntemler:** Sağlık Bilimleri Üniversitesi, Adana Şehir Eğitim ve Araştırma Hastanesi KBB polikliniğinde Ekim 2017-Eylül 2020 tarihleri arasında derin boyun enfeksiyonu tanısıyla hastaneye yatırılıp tedavi edilen 36 hastanın bilgilerine ulaşıldı.

**Bulgular:** Hastaların yaşları 19-73 arasında olup, ortalaması  $41 \pm 14.433$ 'tü. Yaş arttıkça tedavi süresi uzadı izlenmiştir. Ampirik tedavide meropenem 1 (%2.8), ertapenem 1 (%2.8), seftriakson + metronidazol 6 (%16.7), ampisilin sulbaktam + klindamisin 26 (%72.2), ampisilin sulbaktam 2 (%2.8) hastada tercih edilmiştir. Otuz (%83.3) hastanın apse odağı drene edilirken, 6 (%16.7) hasta izole medikal tedavi almıştır. En sık etkilenen bölge submandibuler alanda olduğu izlendi (%47.2).

**Sonuç:** Ampirik ampisilin sulbaktam + klindamisin tedavisinden başarılı bir yanıt alındığını düşünüyoruz.

**Anahtar Kelimeler:** Boyun, bakteriyel enfeksiyonlar, apse, antibakteriyel ajanlar, yetişkin

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Received: 19.11.2021

Accepted: 20.01.2022

Available Online Date: 26.01.2022

## INTRODUCTION

Deep neck infection (DNI) is defined as an infection in the potential spaces and fascia of the neck (1). Before the widespread use of antibiotics, about 70% of DNIs were caused by the spread of tonsillar and pharyngeal infections. Today, tonsillopharyngitis continues to be the most common cause of DNI in children, while odontogenic infections are the most common cause in adults. DNI is an Otorhinolaryngology (ENT) emergency that needs to be treated early and effectively (2). They most commonly develop due to tonsillopharyngitis and odontogenic reasons. DNIs are infections that affect all ages, are difficult to diagnose due to differences in location, and have a high risk of complications (3). DNI has significant morbidity and mortality rate (4).

## MATERIALS and METHODS

The information of 36 patients (15 females and 21 males) in total, who were admitted to the XXXX ENT clinic with complaints such as fever, pain in the throat, swelling in the neck, limitation of neck movements, and pain between 10.01.2017 and 09.01.2020, and were treated with the diagnosis of deep neck infection, and aged between 19-73 years (mean  $41 \pm 14.433$  years), were obtained from their files and evaluated retrospectively. Information such as the duration of the complaint, the antibiotic initiated empirically, the deep neck area involved, the duration of the treatment, additional disease, performing drainage, treatment change were statistically evaluated from the file data. For our study, ethics committee approval was obtained from the University of Health Sciences: Adana City Training and Research Hospital Clinical Research Ethics Committee (Date: 27.02.2020, Meeting Number: 51, Decision No: 739). The study was conducted in compliance with the principles of the 2008 Declaration of Helsinki.

Empirical treatment has been started for patients hospitalized with the diagnosis of DNI in our clinic, and they are given intravenous ampicillin-sulbactam at a dose of 1.5-2 gr four times a day and clindamycin 600 mg three times a day. In case the causative pathogen is detected, specific treatment is started by consulting the infectious diseases.

The correlation between variables was tested with the Pearson Correlation test in cases where the normal distribution assumption was met, and with the Spearman correlation test where the normal distribution assumption was not met. In the comparisons of two independent groups, Student's t-test was used in cases where the normal distribution assumption was met, and the Mann-Whitney U test was used where the normal distribution assumption was not met. In comparisons of more than two independent groups, the One Way Anova test was used in cases where the normal distribution assumption was met, and the Kruskal Wallis H test was used where the normal distribution assumption was not met.

## RESULTS

The ages of the patients ranged from 19 to 73, and the mean age was  $41 \pm 14.433$ . It was observed that the duration of treatment increased with the increasing age ( $p=0.001$ ).

The time between our patients' complaints and their admission to the hospital ranged from 2 to 11 days, with a mean of  $4.97 \pm 2.432$  days.

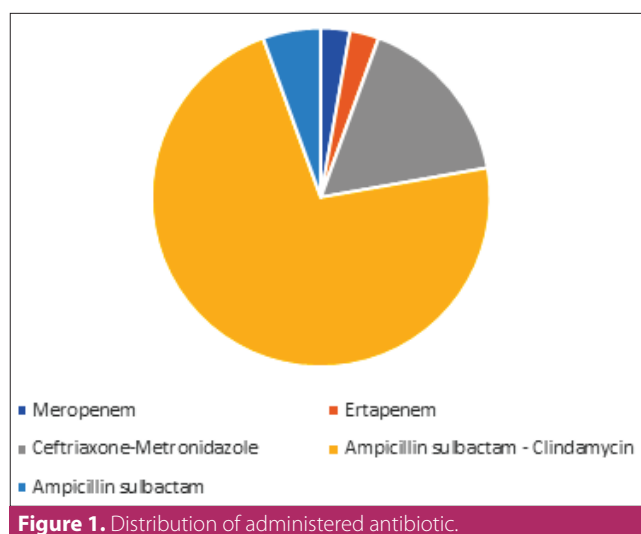
When we look at the DNI location, submandibular abscess was present in 22 (61.1%) patients, parapharyngeal abscess in 3 (8.3%) patients, peritonsillar abscess in 5 (13.9%) patients, parotid abscess in 4 (11.1%) patients, and submental abscess in 2 (5.6%) patients (Table 1).

In empirical antibiotic treatment, 1 (2.8%) patient was initiated meropenem, 1 (2.8%) patient ertapenem, 6 (16.6%) patients ceftriaxone + metronidazole, 26 (72.2%) patients ampicillin sulbactam + clindamycin, 2 (5.5%) patients ampicillin sulbactam (Figure 1).

The duration of inpatient treatment ranged from 3 to 28 days with a mean of  $9.28 \pm 6.012$  days. The number of patients with systemic disease Diabetes Mellitus (DM) was 1 (2.8%), DM + Hypertension (HT) was 1 (2.8%), the pregnant patient was 1 (2.8%), patients with a history of malignancy was 4 (11.1%), the number of patients without any additional disease was 29 (80%). No statistically significant correlation was found between the presence of systemic disease and the duration of treatment ( $p=0.610$ ).

**Table 1.** Distribution of deep neck infections by location

The location of the abscess	Number of patients	Percentages
Peritonsillar abscess	5	13.9
Submandibular abscess	22	61.1
Submental abscess	2	5.6
Parotid abscess	4	11.1
Parapharyngeal abscess	3	8.3
Total	36	100



**Figure 1.** Distribution of administered antibiotic.

While drainage was applied to 30 (83.3%) of the patients, 6 (16.7%) did not require drainage. It was found that there was no statistically significant correlation between drainage and duration of treatment ( $p=0.233$ ).

The empirical treatment of two of the patients (5.6%) was changed, the treatment initiated in 34 (94.4%) patients was continued and the treatment was provided in the patients.

No statistically significant correlation was found between the duration of the treatment applied and the change in the empirical treatment ( $p=0.063$ ).

There was no statistically significant correlation between the antibiotic treatment initiated empirically and the length of hospitalization ( $p=0.281$ ).

In aspirate cultures, streptococcus growth was observed in 3 (10%) of 30 patients drained, and staphylococcus growth was observed in 3 (10%) of them.

There was no statistically significant relationship between the DNI location and the total treatment time ( $p=0.199$ ).

## DISCUSSION

Deep neck infection is an ENT emergency in which it should be diagnosed quickly, hospitalized and treated, and complications may result in mortality. It is a disease that can heal without complications when the treatment is performed quickly, and when abscess formation is seen, surgical drainage should be applied in addition to parenteral antibiotherapy. In the study of Huang et al. in 2004, it has been reported that of a total of 185 DNI patients, 109 were male and 76 were female and peaked in the fifth decade (5). In the study of Ungkanont et al. in 1995 conducted with the pediatric age group, there have been 58 (67.4%) male and 28 (32.6%) female patients (6). In our study, 21 (58.3%) of our 36

patients were male and 15 (41.7%) were female. In our study, the ages of the patients ranged from 19 to 73, and the mean age was  $41 \pm 14.433$ . It was found that there was a significant correlation between the age of the patients and the duration of treatment ( $p=0.001$ ). The duration of treatment was observed to be increased as the age increased.

In the study of Ungkanont et al. in 2004, the three regions where DNI was most frequently located have been reported as peritonsillar, retropharyngeal, and submandibular regions, respectively (6). In our study, when we look at the involvement in DNI, submandibular abscess was found in 22 (47.2%) patients, peritonsillar abscess in 5 (13.9%) patients, parotid abscess in 4 (11.1%) patients, parapharyngeal abscess in 3 (8.3%) patients, submental abscess in 2 (5.6%) patients, respectively.

In the study conducted by Tuna et al. in 2008 with 63 patients, it has been reported that Type 2 Diabetes Mellitus (DM) was seen in 4 (6%) of the patients and 2 (3%) of the patients received immunosuppressant drugs (7). It has been determined in many studies that DM is the most common systemic additional disease in patients with DNI and it has been seen between 50-80% (5,8,9). In our study, the number of patients with DM was 1 (2.8%), the number of patients with DM + HT was 1 (2.8%), the number of pregnant patients was 1 (2.8%), the number of patients with a history of malignancy was 4 (11.1%), the number of patients without any additional disease was 29 (80%). No statistically significant correlation was found between the presence of systemic disease and the duration of hospitalization ( $p=0.610$ ).

When we look at the literature, it is recommended to start the empirical therapy of DNI with an antibiotic effective against commonly isolated aerobic and anaerobic bacteria. Penicillin combined with beta-lactamase inhibitor (such as amoxicillin or ticarcillin with clavulanic acid) or antibiotics resistant to beta-lactamase (such as ceftiofime, cefuroxime, imipenem or meropenem) and drugs (such as clindamycin or metronidazole) that are highly effective against most anaerobes can be used. Vancomycin therapy should be considered for empirical therapy in intravenous drug addicts at risk for MRSA infection and in patients with deep neutropenia or immune dysfunction. Ceftriaxone and clindamycin can be used as empirical therapy against community-acquired MRSA. Ceftriaxone and clindamycin can be used as empirical therapy against community-acquired MRSA in young children to ensure adequate coverage and avoid vancomycin resistance (10-14).

In the study by Hacı et al. examined 85 DNI in 2016, it has been stated that ampicillin sulbactam was used most frequently as an antibiotic and treatment has been performed

by combining metronidazole or clindamycin in many cases (15). In the study conducted by Bal et al with 74 patients with DNI in 2020, it has been stated that 49 patients were treated with paraneural ampicillin sulbactam and clindamycin treatment (16). In our study, in the empirical antibiotic treatment, 1 (2.8%) patient was initiated meropenem, 1 (2.8%) patient ertapenem, 6 (16.6%) patients ceftriaxone + metronidazole, 26 (72.2%) patients ampicillin sulbactam + clindamycin, 2 (2.8%) patients ampicillin sulbactam. The empirical treatment of 2 of the patients (5.6%) was changed, the treatment initiated in 34 (94.4%) patients was continued and the treatment was provided in the patients. One of the patients whose treatment was changed since the empirical treatment could not provide improvement clinically, was diagnosed with mucormycosis and the other was diagnosed with tuberculosis, and their treatments were arranged and cured. In our study, while drainage was applied to 30 (83.3%) of the patients, 6 (16.7%) did not require drainage.

Blood culture is a routine laboratory test in acute febrile illness, but a low rate of positive culture (15.5%) has been demonstrated in deep neck infection. It has been emphasized that abscess culture is a more important test than blood culture (17). In the study of Bal et al. (16), growth has been detected in 85% of the abscess cultures of the patients, and it has been stated that the positivity in the culture results could increase if the anaerobic bacteria culture was performed under appropriate conditions.

In a study conducted by Kataria et al. with 76 patients in 2015, it has been reported that 50% of staphylococci and streptococci were grown in culture (18). In our study, in aspirate cultures, streptococcus was grown in 3 (10%) of 30 patients drained, and staphylococcus was grown in 3 (10%) of them.

DNI can cause life-threatening complications such as upper airway obstruction, mediastinitis, internal jugular vein thrombosis, septic embolism, carotid artery rupture, ARDS, sepsis, and diffuse intravascular coagulopathy (5). In our study, no DNI complications were observed. We think that this may be due to the lack of patients with paravertebral and retropharyngeal abscesses.

Based on our study, we think that a prospective study in which the number of patients was increased and a planned study consisting of groups that were given only ampicillin + sulbactam, clindamycin, and ampicillin sulbactam + clindamycin treatment would contribute more to the literature.

In our study, since it was observed that the duration of treatment increases as the age increases, we think that the treatment period may be prolonged in the treatment of el-

derly patients, although clinical improvement is taken into consideration, and a successful response was obtained from the empirically initiated ampicillin sulbactam + clindamycin treatment. However, we think that in cases where clinical improvement cannot be achieved with empirical treatment, there may be other underlying etiological factors such as fungal, tbc, and malignancy, and examinations for these diseases should be performed immediately.

### Limitations

The limitation of our study is that aerobic and anaerobic cultures were not studied in the patients. There is no conflict of interest in our article.

### CONCLUSION

Although we think that empirical ampicillin sulbactam + clindamycin treatment was successful in our patients due to the absence of prevertebral and retropharyngeal area involvement and no complications, in case of prevertebral and retropharyngeal area involvement and complications, it may be necessary to start a different treatment, which is deemed appropriate, in consultation with the relevant infectious diseases specialist.

### Acknowledgement

We would like to express our special thanks to our dear teacher, Associate Professor Gökhan Kuran.

**Ethics Committee Approval:** This article was approved by the ethics committee of Adana City Training and Research Hospital Clinical Research Ethics Committee (Date: 27.02.2020, Meeting Number: 51, Decision No: 739).

**Author Contributions:** Concept/Design: All of authors; Analysis/ Interpretation: All of authors; Data Acquisition: All of authors; Writing: All of authors; Critical Revision: All of authors; Final Approval: All of authors.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

**Financial Disclosure:** No financial support was received.

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