

ANTIBACTERIAL ACTIVITY OF BUPIVACAINE

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SUMMARY : *In order to investigate the antimicrobial effect of bupivacaine (without any preservative substance) against coagulase negative Staphylococcus (n=53), coagulase positive Staphylococcus (n=28), E.coli (n=28), Klebsiella enterobacter (n=28) and Proteus species (n=28) which were isolated from clinical specimens; minimal inhibitory concentrations were detected using the microdilution method.*

Subclinical concentrations of bupivacaine used in the test were 0.039, 0.078, 0.156, 0.312, 0.625, 1.25, 2.5 and 5 mg/ml. Antibacterial effect (minimal inhibitory concentration) was detected at 0.312 mg/ml for coagulase negative Staphylococcus, 0.078 mg/ml for coagulase positive Staphylococcus, 2.5 mg/ml for Klebsiella enterobacter and E.coli and 5 mg/ml for Proteus species. In our study it was determined that bupivacaine had antibacterial effect against 85 % of the bacterial strains tested.

Key Words : *Local Anaesthetic, Bupivacaine, Bacteria, Antibacterial Activity.*

INTRODUCTION

Some investigators (Grimmond and Brownridge, 1986; Miller and Shelley, 1985; Rosenberg and Renkonen, 1985; Schmidt and Rosenkranz, 1970) studied the antibacterial effect of many different local anaesthetics since antibacterial effect of local anaesthetics was stated long ago (Jonnesco, 1909). However, the investigations about the antibacterial effect of bupivacaine which is a long-acting and widely used local anaesthetic are limited. In all of these studies clinical concentrations of bupivacaine were used. In our study we used subclinical concentrations in order to determine at which concentration this antibacterial effect starts. For this reason, we used bacterial strains isolated from clinical specimens to detect the minimal inhibitory concentra-

tion (MIC) of bupivacaine using the in-vitro microdilution method.

MATERIALS AND METHODS

The strains tested were 53 strains of coagulase negative Staphylococcus (CNS), 28 strains of coagulase positive Staphylococcus (CPS), 28 strains of E.coli, 28 strains of Klebsiella enterobacter (K.ent), 13 strains of Proteus species (P.sp.). The local anaesthetic used was bupivacaine HCl 0.5 % which contained no preservative substance.

Sterilised flat bottomed microplates and Mueller-Hinton broth were used. The bacterial inoculum was standardised according to 0.5 Mc Farland (Baron and Finegold, 1990).

Microdilution method was used in ten wells. Se-

rial dilution was performed from first to 8th well. 9th and 10th wells were used as positive and negative controls. With this method the concentrations of bupivacaine were 5, 2.5, 1.25, 0.625, 0.312, 0.156, 0.078 and 0.039 mg/ml.

After incubation at 37°C for 24 hours, the minimal concentration of bupivacaine that inhibited the growth of bacteria was determined as the MIC value (NCCLS, 1988).

RESULTS

As seen in Table 1, the antibacterial effect of bupivacaine started at the concentrations of 0.312 mg/ml for CNS, 0.078 mg/ml for CPS and 2.5 mg/ml for K.ent., E.coli and 5 mg/ml for P.sp.. The percentages of resistant strains were 1.88 % in CNS, 7.1 % in CPS, 21.4 % in E.coli, 25 % in K.ent.

and 53.9 % in P.sp. (Fig 1). Bupivacaine had antibacterial effect against 85 % of all the strains.

Bacterial growth was observed in the 9th well, whereas no growth was observed in the 10th well which were used as controls.

DISCUSSION

In the beginning of nineteenth century, besides their analgesic and anaesthetic properties, antibacterial effect of local anaesthetics were also mentioned (Jonnesco, 1909). Until today, the antibacterial effects of many different local anaesthetics were investigated, but the studies about bupivacaine were limited (Grimmond and Brownridge, 1986; Miller and Shelley, 1985; Noda et al. 1990; Rosenberg and Renkonen, 1985).

In one of the studies, it was stated that the anti-

Species of bacteria	Doses of Bupivacaine (mg/ml)								No. of resistant strains
	0.039	0.078	0.156	0.312	0.625	1.25	2.5	5	
CNS (n=53)	+	+	+	1*	1	17	32	1	1
CPS (n=28)	+	1*	2	2	8	8	4	1	2
E. coli (n=28)	+	+	+	+	+	+	16*	6	6
K. ent. (n=28)	+	+	+	+	+	+	15*	6	7
P.sp. (n=13)	+	+	+	+	+	+	+	6*	7

(+) Growth Observed (*) MIC Values

Table - 1 : The in - vitro inhibition values of tested bacteria to different doses of bupivacaine.

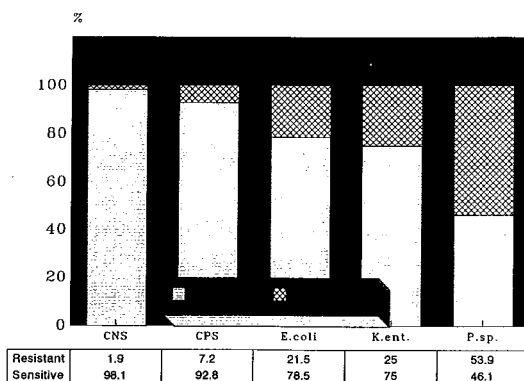


Fig 1 : The susceptibility percentages of different bacteria to bupivacaine.

bacterial effect started at the concentration of 2.5 mg/ml and the concentration of 5 mg/ml inhibited all the strains tested except P. aeruginosa (Rosenberg and Renkonen, 1985). In another study, it was detected that the inhibition started at 3.75 mg/ml (Noda et al. 1990). And it was also indicated that the antibacterial property of bupivacaine was effective at body temperature. In addition to this, it was mentioned that this effect might be a factor keeping the epidural catheters sterile during their continuous usage (James et al. 1976).

In this study, we demonstrated that antibacterial effect of bupivacaine has started at concentrations lesser than the clinic concentrations. Bupivacaine inhibits 85 % of the tested bacterial strains at the concentration of 5 mg/ml. Thus the increase in concentration made the agent more potent and this was concordant with other authors' results (Grimmond and Brownridge, 1986; Miller and Shelley, 1985; Noda et al, 1990; Rosenberg and Renkonen, 1985).

Although the mechanism of the antibacterial effect of local anaesthetics have not been clearly understood yet, they may be acting through various mechanisms like inhibiting cell wall synthesis or disturbing the function of cytoplasmic membrane. As an example it was stated that neither lidocaine nor procaine inhibited the synthesis of proteins, DNA or RNA selectively, but the mechanism of their effect might be related to bacterial wall and cytoplasmic membrane structure (Schmidt and Rosenkranz, 1970).

It is suggested that the antibacterial effects of local anaesthetics have to be considered when there were false negative culture and skin biopsy results after the application of local anaesthetics (Miller and Shelley, 1985).

As there are some bacterial strains inhibited by bupivacaine which are generally resistant to antibiotics, the value of our results is important. This antibacterial effect of bupivacaine may provide a protection against infections when used in different clinical applications, as stated by some other authors.

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