AN EVALUATION OF ETIDOCAINE (DURANEST®): A NEW LOCAL ANAESTHETIC AGENT

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LIDOCAINE was synthesized in 1943 by Loffren, and introduced as the first local anaesthetic agent having an amide between the lipophilic aromatic residue and the intermediate chain.

In some circumstances, it would be preferable to have an anaesthetic drug with longer duration of action than lidocaine, but without increased toxicity. We have previously reported^{8,10} on the use of a long acting compound. Prolanest®, which is prilocaine bound physically to polyvinylpyrrolidone (PVP), Plasdone C, molecular weight 40,000).

Two new amides, bupivacaine and etidocaine^{2,4,6} have recently been introduced as local anaesthetic agents with prolonged duration of action. In the present investigation we have compared the activity of etidocaine with lidocaine.

The investigation was carried out on patients and was limited to a controlled clinical evaluation of the activity of etidocaine (W-19053) on A and C fibres, compared to the activity of lidocaine.

Drug concentrations studied were etidocaine 0.25 per cent, 0.50 per cent and 1 per cent with epinephrine. For the purposes of this report only the data on the 1 per cent concentration were compared with lidocaine 1.5 per cent with epinephrine.

The present investigation of etidocaine was designed to determine optimal and safe volumes to be used in epidural analgesia, to compare the rate of onset of anaesthesia, establishment of maximum anaesthesia and regression of anaesthesia, and to compare the toxicity and safety of etidocaine with lidocaine.

Etidocaine has also been used for brachial blocks and therapeutic blocks, but these data are not presented in this study.

The chemical structures of etidocaine and lidocaine may be compared in Table I.

METHODOLOGY

The study was carried out in 40 patients who were to receive peridural anaesthesia for various operations (Table II).

These were divided into two matched groups and randomly allocated to receive 1 per cent etidocaine with epinephrine (1:200,000) or 1.5 per cent xylocaine with epinephrine (1:200,000).

The characteristics of the two groups are compared in Table III.

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TABLE I

1. LIDOCAINE (XYLOCAINE 'R')

2. ETIDOCAINE (DURANEST 'R')

TABLE II
LIST OF SURGICAL PROCEDURES

Operation	Etidocaine	Lidocaine
Herniorraphy	8	8
Vaginal hysterectomy	4	3
Stripping of saphenous vein	1	2
Meniscectomy or arthrotomy of knee	5	5
Arterial graft	1	1
Open reduction	1	1
Total	20	20

TABLE III
LIDOCAINE VS ETIDOCAINE
COMPARISON BETWEEN THE TWO GROUPS OF PATIENTS

	Lidocaine 1.5%	Etidocaine 1%	T-Test
Age:			
Mean	44.9	45.2	
S.D.	17.13	17.27	T = 0.06
Variance	293.46	264.59	P > 0.05
S.E.	3.83	3.64	Not Significant
Number	20	20	
Weight (pounds):			
Mean	153.5	149.5	
S.D.	42.65	27.55	T = 0.37
Variance	1 819.42	758.53	P > 0.05
S.E.	9.54	6.16	Not Significant
Number	20	20	
Risk (ASA):			
Mean	2	2	
S.D.	0.89	0.83	T = 0.55
Variance	0.79	0.69	P > 0.05
S.E.	0.2	0.19	Not Significant
Number	20	20	
Time for Surgery (min):			
Mean	97	132.75	
S.D.	22.5	71.18	T = 2.14
Variance	506.32	5 067.04	P < 0.05
S.E.	5.3	15.92	Significant
Number	20	20	

PREMEDICATION

Pre-operatively all patients received diazepam 15 mgs and atropine 0.4 mgs, half an hour before induction of peridural anaesthesia with the assigned agent.

The majority of patients also received a further reinforcing dose of diazepam 5 mgs or Innovar® 1.01 ml before anaesthesia.

DETERMINATION OF ONSET, MAXIMUM ANAESTHESIA AND REGRESSION

The evaluation of anaesthetic activity of the agent was done objectively by assessing the loss of sensation and motor function using the criteria described by Bromage¹.

The duration of anaesthetic activity was judged by the return of motor function to Grade 1 using the same criteria.

Blood Examinations

We also attempted to assess toxic side reactions, by examination of blood samples for cellular contents, enzyme activity and formation of methaemoglobin.

The enzymes measured were the serum glutamic-oxaloacetic-transaminase (SGOT), the serum glutamic-pyruvic-transaminase (SGPT), the creatinine phosphokinase (CPK), the lactic dehydrogenase (LDH) and plasma cholinesterase.

To determine these enzymes, a spectrophotometer UNICAM was used and the technique was employed with a standard deviation.

"Student's T Test" was used for evaluation of results.^{7,12}

Dose

The dose injected, onset of anaesthesia and duration of anaesthesia for lidocaine and etidocaine are listed in Table IV.

The dosage in mgs is smaller with etidocaine, 176 mgs compared to 369 mgs with lidocaine.

The mean dose in mgs required for satisfactory anaesthesia with etidocaine, was about 50 per cent of the dose of lidocaine required to produce similar anaesthesia.

Onset

The time to onset of anaesthesia with etidocaine was less than half of that for lidocaine, being 5 minutes as compared to 13.4 minutes for lidocaine.

The time required for attainment of satisfactory sensory and motor loss was significantly shorter.

Duration

The duration of anaesthetic activity judged by return of motor function to satisfactory level, was significantly longer ($p < 0.01$) with etidocaine when compared to lidocaine. The longest duration was seven hours and eight minutes and the shortest 2 hours 40 minutes.

TABLE IV
RESULTS LIDOCAINE VS ETIDOCAINE COMPARISON OF THE TIME OF ACTION

	Lidocaine 1.5% Epi 1:200 000	Etidocaine 1% Epi 1:200 000	T-Test
MG Injected:			
Mean	369	176.75	
S.D.	56.84	33.96	T = 12.99
Variance	3 230.53	1 153.36	P < 0.01
S.E.	12.71	7.59	Highly Significant
Number	20	20	
Onset (min):			
Mean	13.4	5.7	
S.D.	1.73	2.99	T = 9.97
Variance	2.99	8.96	P < 0.01
S.E.	0.39	0.67	Highly Significant
Number	20	20	
Sensitivity Complete Loss (min):			
Mean	16.9	12.55	
S.D.	1.94	3.2	T = 5.2
Variance	3.78	10.26	P < 0.01
S.E.	0.43	0.72	Highly Significant
Number	20	20	
Motricity Complete Loss (min):			
Mean	17.7	14.4	
S.D.	1.84	5.25	T = 2.66
Variance	3.38	27.41	P < 0.05
S.E.	0.41	1.17	Significant
Number	20	20	
Motor Return (min) Grade 1:			
Mean	168.25	270.16	
S.D.	32.58	74.96	T = 5.56
Variance	1 061.25	5 618.81	P < 0.01
S.E.	7.29	17.2	Highly Significant
Number	20	19	

Blood Examinations

No significant changes were observed in the haematocrit or sedimentation rate operation when compared with preinduction values. Slight augmentation of LDH was noted at four hours, but this returned to normal within 24 hours.

Complications and Side Effects

There were no major complications.

We observed one case of shivering with etidocaine and no case with lidocaine.

Three patients complained of pinching sensation at the beginning of injection.

A small degree of hypotension occurred once in the series with etidocaine and three times with lidocaine.

One instance of extrasystole occurred six hours after peridural anaesthesia with etidocaine and there was one similar instance one hour after lidocaine, but this is not significant.

Two cases of anxiety due to the long duration were observed in the recovery room after etidocaine.

There was only one case of unsatisfactory anaesthesia with etidocaine, compared to three cases with lidocaine.

DISCUSSION

This study has permitted us to compare the relative advantages of etidocaine for use as a local anaesthetic agent for peridural block, especially for use during protracted operations. The superiority of etidocaine in the duration of anaesthetic activity is clearly demonstrated and this eliminates the necessity for reinforcing doses for prolongation of anaesthesia.

The attainment of sensory and motor anaesthesia in all patients (19 of the 20 cases), in the present series, was satisfactory with etidocaine 1 per cent with 1:200,000 epinephrine. No reinforcing doses were required, although the mean duration of the operations was 2 hours and 15 minutes for the cases done under etidocaine anaesthesia, compared to 1 hour and 37 minutes with lidocaine.

The onset of anaesthesia as judged by sensory loss, was twice as fast with etidocaine as with lidocaine.

The safety of the drug is well demonstrated.

As judged from the serum enzyme studies, we have not observed any toxic reactions.

Elevation of the CPK is not significant as this elevation is often found after prolonged operations when other anaesthetic agents are used, or even after a small muscle trauma such as intramuscular injection, due to the abundance of this enzyme in the muscle.

During the 24-hour period following anaesthesia, no untoward vasomotor or other undesirable side effects were observed, except one case of extrasystole.

There was no formation of methaemoglobin such as is found with prilocaine.

DURATION OF ANAESTHESIA

The duration of etidocaine is at least twice as long as lidocaine on A and C nerve fibres. It is desirable for long surgical operations.

CONCLUSION

In conclusion, it may be stated that etidocaine, by virtue of its prolonged anaesthetic activity and freedom from undesirable toxicity and side effects, is a useful addition to the therapeutic armamentarium of an anaesthetist.

RÉSUMÉ

Une évaluation clinique de l'activité comparative de l'étidocaïne et de la lidocaïne est présentée. Deux groupes de 20 malades chacun ayant reçu une anesthésie péridurale ont été étudiés.

La supériorité de l'étidocaïne, surtout en ce qui a trait à la durée d'action, en fait un agent utile dans les interventions de longue durée.

GENERIC AND TRADE NAMES OF DRUGS

Etidocaine – Duranest

Lidocaine – Xylocaine

Prilocaine – Citanest

Prolanest – Citanest and Plasdone C

Diazepam – Valium

Epinephrine – Adrenaline

Bupivacaine – Marcaine

Sublimaze (Fentanyl), Inapsine (Droperidol) – Innovar

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