LIGNOCAINE: ITS USE IN VENTRICULAR ARRHYTHMIA (Except VF) FOLLOWING ACUTE MYOCARDIAL INFARCTION*

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Introduction

LIGNOCAINE, a local anaesthetic synthesised by Lofgren in 1943 was first introduced as an antiarrhythmic agent in 1950 by Southworth et al. Since then it has been successfully used in the management of ventricular arrhythmia from various causes (Harris et al 1956; Bedyneck et al, 1966). Recently it has been recommended as a treatment of choice in the ventricular arrhythmia following acute myocardial infarction (Harris et al 1956; Bedyneck et al, 1966;) Even routine prophylactic administration of this drug in this disease in the patients' home by the general practitioner has been advocated (Harris et al, 1956; Bedyneck et al, 1966;) Its effectiveness is now fully assessed but its side effects are not often very well appreciated (Harris et al 1956; Bedyneck et al 1969;

I would like to describe here my experience with the use of this drug in the treatment of ventricular arrhythmias (except VF) following acute myocardial infarction in a 4 bedded Intensive Coronary Care Unit in Sefton General Hospital. We have been using lignocaine since 1967, but for the purpose of this study I have taken only those cases admitted since October, 1968 to April, 1969. The set of the unit is similar to one described by Aber et al, 1969.

Method of Lignocaine Administration

Lignocaine is used mainly in the management of ventricular premature beats (VPB) and ventricular tachycardia (VT). VPB are treated only if the ectopics are multifocal, or if it occurs at more than five per minute, or if it falls on the T wave of the preceding QRS complex (Aber et al, 1979). Succession of three or more consecutive ventricular premature beats occurring usually at a rate of the 150 to 200 per minute is taken as ventricular tachycardia (Aber et al, 1969).

Lignocaine is used as a drug of first choice. A starting dose of 1mg/kg body weight (average dose: 50 to 70mg) intravenously is used. After a starting dose the drug is maintained by a continuous infusion at the rate of 1 to 2mg per minute. If the arrhythmia is well controlled an attempt is made over next 6 to 12 hours to reduce the infusion dose by 1mg/mt and finally it is discontinued. The average total duration of lignocaine therapy was two days. If the frequent VPB persists or reoccurs the dose is increased by 1mg/mt

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upto maximum of 4mg/mt. (If there is sudden increase in the frequency of the VPB or develop VT, an additional stat dose of 40 mg is given intravenously. If the arrhythmia is suppressed to only occasional VPB (less than 1-2 per minute) no additional antiarrhythmic treatment is considered necessary. In the event of the development of side effects the infusion is stopped for 10 minutes and then continued again at a dose reduced by 1mg/mt.

Those patients whom we think will need antiarrhythmic treatment for more than 3 or 4 days are put on oral procaine amide and weaned off lignocaine before discharge from the unit to the general medical ward. This group includes those patients who had VT, or frequent or multifocal VPB after resuscitation from cardiac arrest, especially VF and those still having occasional VPB after maximum dose of lignocaine on second or third day of admission. It is our practice to keep them on oral procaine amide for at least further two to three weeks.

Lignocaine is available in 5ml ampules of 2% solution for use as a stat dose. Our Pharmacy also makes 500ml infusion bottles containing 60mg, 120mg, 180mg and 240mg per 30ml dextrose each, which when given at 30ml per hour give concentration of 1,2,3, and 4mg per minute respectively.

All our patients now have a Central venous catheter inserted by Seldinger technique or a cut down in the Median Cubital Vein. This is used for administration of drugs, measuring Central Venous Pressure (CVP), and for withdrawing blood for biochemical tests. It is also used for recording Rt. atrial ECG in case of difficult arrhythmias. The line is kept open by a slow dextrose drip. Lignocaine when indicated is administered through this line. The infusion set we use for administering lignocaine is a 'Disposable Recipient Set for Infants (Capon Heaton & Co. Ltd; Eng.). It has a 30ml measuring chamber and two plastic 'Flow Control' clip. The measuring chamber is filled every hour, and the lower "Flow Control" is adjusted to give infusion at 30ml/hr. The result of lignocaine therapy is assessed as follows:-

GOOD: If the arrhythmia is suppressed completely, or if the frequency of VPE is decreased to only occasional ones, requiring no further additional anti-arrhythmic treatment; and if there is no occurrence of VT during the period of therapy.

FAIR: Arrhythmia well controlled but developed serious side effects necessitating the dose of lignocaine and addition of other antiarrhythmic drugs e. g. procaine amide.

FAILURE: No effect on the arrhythmia, or effective suppression of VPB but developed VT while on it; if VPB suppressed, still more than 5 per minute.

Results

Since October 1968 to 15th April 1969 150 patients had 162 admissions; out of them 114 had acute myocardial infarction (52 had posterior infarct, 52 anterior, 3 subendocardial and site not known in other 7. In those with anterior infarct it was mainly antero-septal in 30 out of 52).

Ventricular Premature Beats

Seventy (61.5%) had VPB, 55 of whom needed treatment with lignocaine. Control of the arrhythmia was good in 34(61.8%), fair in 3 and failure in 18(32.7%). Among those in whom lignocaine failed to control the arrhythmia 5 were getting the drug at 4mg/mt, 3 on 3mg/mt, 5 at 2mg/mt and the rest at 1mg/mt. Three died while on 1-2mg per minute and arrhythmia still uncontrolled, 3 developed side effects at 2mg/mt necessitating a decrease the infusion dose to 1mg/mt, and addition of procaine amide to control the arrhythmia. Others at 1-3mg/mt were regarded failure as the repeated stat dose failed to affect the arrhythmia.

Ventricular Tachycardia

Twenty three patients had among them 46 episodes of VT, including one with Acute myocarditis who had 16 episodes in two days. Only 17 patients out of 23 had definite acute myocardial infarction (15.5%).

These 17 with Acute Myocardial Infarction had together 26 episodes of VT. Two had 4, 4 had 2 and the rest had one episode respectively. Twelve of them (15 episode) developed VT on the first day of infarct, and rest within first four days except one who had reoccurrence on the 7th day and another on the 3rd week of infarct.

Ventricular Tachycardia lead to VF on 6 occasions in 4 patients. All of them were receiving lignocaine. Out of 25 episodes (in Acute Myocardial Infarction Group) the control of the arrhythmia was good only in 10(40%). Rest 6 who had VT, 5 had ischaemic heart disease and paroxysmal VT but no evidence of recent infarct and the sixth had Acute Myocarditis (Autopsy Diagnosis.). Lignocaine was used without effect on 2. The arrhythmia was controlled either with oral procaine amide or quinidine in all except one with myocarditis who died.

Side Effects

Fourteen out of 62 of our patients who received lignocaine (22.5%) developed cerebral symptoms attributed to this drug. Three got symptoms on more than one occasion, two had three episodes and one had two episodes. Seven were receiving lignocaine at 4mg/mt, 3 at 3mg/mt, 5 at 2mg/mt and rest 1 at 1mg/mt.

Objective Symptoms

Six got convulsion, one on two occasions, four of these were on 4mg/mt, one on 3mg/mt and rest on 2mg/mt. Focal twitching were noted in five, one developed on three occasions. Three lost consciousness temporarily, two while at 4mg/mt and the third did so on three occasions while at 2mg/mt. Four became very confused while on lignocaine, three got slurred speech. Sweating, moving of head from side to side, hyperventilation and restlessness and irritability were noted in two each. One developed hysterical behaviour. Subjective symptoms: Three complained of sweating, two of blurred vision, one of diplopia and of objects moving from side to side in the centre of vision. Two felt very odd while on lignocaine infusion, two complained of being dizzy and light headed and one of less power and weakness in hands.

These symptoms usually last for about 8 to 10 minutes and the recovery is complete on temporarily discontinuing the infusion. After 5-10 minutes we usually restart the drip at a rate reduced by 1mg/mt. Most often this is all that is required to alleviate these symptoms. But sometimes we have used Sodium Phenobarbitone 200mg. or Diphenylhydantoin (Dilantin) 100 to 200mg Intravenously in case of convulsion. This procedure is perhaps unwanted and could be harmful (Vide Infra).

I have seen four patients develop convulsion while on lignocaine given for VT after resuscitation from VF. They are not included in this series because of this the possibility of being due to cerebral hypoxia. It is however possible that hypoxia may potentiate the cerebral toxicity of this drug. Sudden development of the symptoms are often very alarming to the patient. Some of the cases are described below.

Case 1. Mrs. E.D. (47 yrs):-

On 2mg/mt infusion. For sudden increase in the frequency of VPB. was given a stat dose of 50mg lignocaine. She suddenly lost consciousness. Twitching of fingers were noted. Breathing deeply. Did not response to painful stimuli. Deep reflexes were normal. In sinus tachycardia (126/minute), BP, 140/90 (her PR and BP) of before and after this episode was 100 and 100/70 respectively). She recovered completely within 10 minutes.

Next day, while still on 2mg/mt she suddenly developed symptoms as before, following which the dose was reduced to 1mg/mt.

However on the 3rd day she again got frequent VPB and the lignocaine was increased to 2mg/mt. The arrhythmia was well controlled but within a few hours she suddenly developed convulsion, lost consciousness and had focal twitchings. Recovered completely in about 10 minutes. This patient was put on oral procaine amide and lignocaine was withdrawn gradually.

Case 2. A.C. (30 yrs): Paroxysmal VT.

On lignocaine 4mg/mt. Suddenly complained of lightheadedness, dizziness and blurred vision. Speech was slurred. Was alarmed by the sudden development of the symptoms. He understood all questions put to him and replied rationally, but speech was slow and slurred and says he had difficulty to use the correct expression. Hearing was good and he was very much aware of the surroundings and of 'the funny state' he was in. Recovered completely in 10 minutes. Later was fully aware of the state and the speech but was unable to control it. The rate of lignocaine infusion was reduced to 3mg/mt.

Five hours after the first episode, he suddenly developed convulsion. Remained fully conscious, got symptoms as before. Recovery was complete on discontinuing the infusion. As the drug was not effective in controlling the arrhythmia it was gradually withdrawn.

Case 3: J. M. (55 yrs)

On lignocaine 3mg/mt infusion. Dose increased to 4mg/mt because of frequency of VPB. One hour later the patient was noticed moving his head from side to side. He was unco-

nsconscious, not responding to painful stimuli. There was some increase in tone of the muscles of neck, jaw and upper extremities. Deep jerks including plantars were normal and no focal twitching of the eyelid or fingers were noted. He came round in about 8 minutes and was later unaware of what happened to him.

Case 4 H.P. (63 yrs):-

On 1mg/mt after withdrawing blood samples for biochemical tests the drip was accidentally left to run a bit faster for a few minutes. He soon complained of feeling drowsy, lightheaded, blurred vision and feeling of weakness of power in hands.

No focal twitching or fasciculation was noted. The dramatic development of the symptoms alarmed and frightened the patient very much. Symptoms rapidly cleared on stopping the drip for a few minutes.

Case 5: B.I. (39 yrs): Ac. Myocarditis.

On 3mg/mt for last 16 hours. He suddenly developed abnormal behaviour. He was moving his head from side to side and was shouting loudly. Repeatedly cried out that he is going to die. He appeared very frightened. He was not known to behave abnormally before. The possibility of it being due to lignocaine was considered and it was stopped and was put on procaine amide.

His third admission to the unit was after resuscitation from VF in medical ward. He was in VT at 250mg/mt. Lignocaine 50mg was given and a repeat dose of 100mg after 10 minutes which converted the rhythm to sinus with occasional short runs of VT. The drug was then maintained at 2mg/mt which had to be increased to 3mg/mt and then to 4mg/mt. Over next few hours repeated attempts were made without success to reduce the dose of lignocaine infusion. After about 12 hours he suddenly started to scream loudly and inbetween was muttering incoherently. He repeatedly tried to get out of bed and had to be restrained; and sedated with Dimorphine. Lignocaine was stopped for a few minutes and continued at 2mg mt. He continued to develop paroxysms of VT which was unresponsive to IV procaine amide and electric cardioversion. Three hours later another attempt was made convert the arrhythmia by lignocaine. A stat dose of 70 mg was given. He immediately developed symptoms like before. His speech was slurred. And after 15 minutes developed convulsion. In one of his paroxysms of VT he went into VF. Was successfully resuscitated. But inspite of the fact that he had immediate, continuous and adequate ventilation and external cardiac massage he did not regain consciousness and died four days later. He continued to receive lignocaine later to control the ventricular arrhythmia till two days before death.

Discussion

Lignocaine (2-diethylamino-2, 6-acetoxy) is a local anaesthetic synthesised by Lofgren in 1943. But the drug was not clinically investigated until 1946 and not generally introduced into medicine until 1948. Lignocaine does not belong to cocaine-procaine group of drugs. Chemically it is an amide, an aminoacyl and a derivative of acetanilide (Foldes 1966; Morris, 1966; Woodsmith et al 1968).

It is very stable, can be stored indefinitely and autoclaved repeatedly. It is extremely to hydrolysis by alkalies and acids (Giddes 1958; Morri 1966; Woodsmith et al. However it should not be left unduly long before use in metal pots or in syringes with metal fittings since it can liberate ions of metals such as copper and nickel (Morris 1966; Woodsmith et al 1968).

It has excellent power of diffusion, and this is responsible for the rapidity of its action. It is metabolised in liver (Giddes 1958; Foldes 1966). The initial step being oxidative deethylation of one of the Nethyl Group followed by hydrolysis of the amide bond (Hollunger, 1960). In vitro incubation of lignocaine C14 with tissue slices from several organs has shown that the liver is the only organ capable of metabolising the drug at significant rate (Chen & Sung 1954; Giddes 1958;). Two medical students receiving 3mg/Kg excreted only 3 and 11% respectively in 24 hours. Ninety percent of the injected dose is metabolised in liver and in urine only 10 percent appearing unchanged in urine. It thus appears that catabolism, as opposed to excretion is the principle means by which body disposes of lignocaine and liver is the most important organ in this respect. The main metabolite of this drug is the diethylaminoacetic acid (Giddes 1958)

Effects of lignocaine on Circulation

Effects of lignocaine on circulation were studied in laboratory animals (Haggart et al, 1951); of Washe et al, 1954 and Austin et al, 1965) and in man (Kimmey & Steinhause, 1959; Harrison et al, 1963) and in patients with acute myocardial infarction (Jewitt et al, 1968). Austen et al (1965) noted that lignocaine injected into the central circuit at a dose of 1mg/kg caused a pronounced fall of myocardial contractility (by 32%), drop in central blood pressure by 18% and fall in heart rate by 8% and little change in femoral pressure. Systemic injection of 2mg/kg caused drop of 20%, in femoral pressure with lesser fall in myocardial contractility and central pressure. Large doses (8 to 15mg/kg) in central flow progressive and profound depression of myocardial contractility and heart rate; cardiac dilation and standstill.

Harrison et al found that lignocaine at dose of 1 to 2 mg/kg produced no significant circulatory depression while every patient given therapeutically. Comparable dose of procainamide (2 to 4mg/kg) showed a fall in arterial pressure and a decrease in contractile force of the right ventricle. The finding of Kimmey and Steinhause (1959, quoted by Jewitt et al) and that of Jewitt et al (1968) are semimillar. After an intravenous injection of 1mg/kg a slight increase in mean arterial pressure and cardiac output was noted in five normotensive patients. However, minor falls in arterial pressure were observed after a simmiller injection of lignocaine in three hypertensive patients. These changes are regarded as being statistically not significant.

Foldes et al (1960) observed flattening and disappearance T wave, depression of ST segment and increase in amplitude of P wave in 30% and no change in ECG in rest 70% after infusion of lignocaine at 0.5mg per minute. Other found no significant change in sinus rate and the QRS complex.

The direct effect of lignocaine on myocardium has been studied and compared with procaine amide in animals and in man (Harrison et al 1963 Austen et al 1965). Both lignocaine

and procaine amid caused elevation in the electric threshold of the ventricle during diastole and neither caused any significant change in the duration of the absolute refractory period (Harrison et al 1963). Washe et al (1953) Harrison et al 1963 have previously observed similar effect with procaine amide. This effect thus may be related to their antiarrhythmic property (Harrison et al 1963). It will however be interesting to recall here the action of lignocaine as a local anaesthetic, which acts effectively only at the nodes of Ranvier where they stabilise the plasma membrane in respect to ionic permeability and in some way that is yet incompletely understood prevent the ionic migration which is essential for conduction in nerve (Morris 1942). It may have similar effect on the myocardium and this may perhaps have more direct bearing on its action as an antiarrhythmic agent.

Lignocaine as an antiarrhythmic agent

It was Southworth et al (1950) who first used lignocaine as an antiarrhythmic drug. They described the successful intracardiac use of lignocaine with procainamide and A.C. Shock to control VF arising during cardiac catheterisation. Harris et al (1956) found it effective in controlling VT following experimental Acute myocardial infarction in laboratory animals. Garden and Steinhaus (1956) used it in the management of ventricular arrhythmias occurring during and after cardiac surgery. Likoff (1959) advocated intravenous use of the drug in the management of various arrhythmias during cardiac surgery and suggested the dose of 1 mg per 2 to 3 lb. body weight. Subsequently it was successfully used in ventricular arrhythmia of non-surgical origin including acute myocardial infarction (Badyneck et al 1966 Gianelli et al 1967; Grossman et al 1967) Hayes et al 1967. Grossman et al (1967) found it effective in the management of ventricular arrhythmias (VPB, VT) but not in atrial or supra-ventricular arrhythmias. Sparcklen et al (1968) has confirmed it and also found it effective to some extent in controlling atrial ectopics. Lown et al (1967) recommended the use of lignocaine for the management of ventricular arrhythmias (VPB, VT) developing from acute myocardial infarction and it is now regarded as a drug of choice for this purpose (Jewitt et al 1968; Killip 1968).

The antiarrhythmic effect of an intravenous injection of lignocaine 1mg/kg lasts for about 15 minutes (Jewitt et al 1964) and the maintenance of continuous suppression of arrhythmia requires continuous infusion of the drug (Stock 1969). Killip (1968) considers a plasma level of lignocaine in excess of 1 µg per ml necessary for antiarrhythmic effect. Jewitt et al regards the antiarrhythmic level to be 1.5 to 2.5 µg per ml. This is achieved by a continuous infusion of lignocaine at 2mg/mt. The incidence of ventricular arrhythmias and the role of this drug in their management in acute myocardial infarction is discussed below.

Ventricular Premature Beats

The incidence of VPB in this series (61.5%) is similar to that reported in the literature (60-80%) (Julian et al, 1964; Meltzer and Kirchell, 1966; Lown et al, 1967).

Haemodynamic effect of VPB are not significant (Julian et al 1964). And in the past there has been tendency to minimise the significance of VPB on the assumption that they are innocuous and did not influence the mortality. Experience with cardiac monitoring has changed this

impression and it is now quite apparent that VPB should not be disregarded. These ectopic contraction seems to reflect the state of myocardial irritability in Acute myocardial infarction and may forewarn a serious ventricular arrhythmias (Meltzer et al 1966). The likelihood of VT or VF is greatly increased if VPB occur at more than 5 per minute, are multifocal, bigemny or it occur on the T wave of the proceeding QRS complex (Julian et al 1964; Meltzer Lown et al 1967) et al 1966. So the main aim of treating VPB is to prevent the development of VT and VF.

Basing our criteria of success on above principal and the maintenance of continuous suppression of VPB, we found lignocaine to be effective only in 61.8%. This figure is lower than reported by 78% Chopra et al 1969.

Other drugs with specific antiarrhythmic property available for management of VPB include quinidine, procainamide, diphenylhydantoin and antazoline. Antazolin is an antihistamine with some pharmacological properties similar to those of quinidine, atropin and procaine. It is a myocardial depressant and it causes marked prolongation of the refractory period of the atrium (Friedberg 1968). As yet we have no sufficient knowledge and experience about this drug as an antiarrhythmic agent. Diphenylhydantoin, long employed as a standard therapy for epilepsy was used in cardiac arrhythmias on the assumption of it being of similar nature to the electrical disturbance as epilepsy. And it has been reported favourably as an antiarrhythmic agent (Bernstein et al 1968), but others found its effectiveness to be variable and undependable (Friedberg 1968). Toxic effect of this drug include widening of QRS complex, prolongation of PR interval, ST-T changes, ventricular extrasystoles and cardiac standstill. Quinidine, the dextro isomer of quinine has been known for its antiarrhythmic property for over 100 years. Its action on heart include depression of excitability, conduction velocity and contractility. It also lowers the peripheral vascular resistance. It is a cumulative drug and large doses give rise to cinchonism and its toxic effect on heart include extrasystoles, atrioventricular and interventricular block, VT, VF and cardiac asystole. Selzer and Wary (1964) has pointed out that "Quinidine Syncope", which in their experience was a common event, was usually due to paroxysmal ventricular fibrillation (BMJ 1968). So procaine amide which is more effective than quinidine in the management of ventricular arrhythmias has gradually replaced it (Friedberg 1968). Procaine amide is effective when given orally or IM or IV. It depresses myocardial excitability and has some adverse haemodynamic effect. Toxic effect includes widening of QRS complex, rarely VT and VF. Prolonged oral use of drug has similar effect as quinidine. Hypotension is a serious complication only when the drug is administered intravenously. And in patient with Acute myocardial infarction this could prove fatal. Lignocaine compares very well with procaine amide as an effective antiarrhythmic agent. It is rapid in its effect and haemodynamically very safe. But it has to be given intravenously and hence not suitable for prolonged use and is more neurotoxic than procaine amide.

Ventricular tachycardia

The incidence of VT in acute myocardial infarction was previously reported as 1% (Mintz and Katz, 1947); Dimond et al, 1960: 3 to 4% (Dreifus et al, 1958); 6% (Julian et al 1964). Cohen et al (1966) found it to be 11% in four collected series and predicted that it could be as high as 60% if continuously monitored. Current studies however indicate it to be about

15 to 20% (Killip and Kimball, 1968). The incidence in this series is 15.5%.

Ventricular Tachycardia in Acute myocardial infarction may be self terminating brief arrhythmia of 4 to 20 successive beats at rate of 70 to 250 per minute or abrupt in onset, rapid in rate and sustained, potentially malignant and seriously compromising systemic pressure and cardiac output and require to be terminated immediately (Lown et al, 1964 1967). Ventricular Tachycardia of any sort carries a very bad prognosis (Julain et al not only because of its deleterious haemodynamic effect (Cordey et al 1959) and death producing on its own but also that VF may develop at any time (Julain et al 1964; Lown et al 1967 Meltzer et al 1966) Three of our patients with VT were admitted in shocked state, and VT lead to VF on six occasion in other four. Because of its grave prognosis in Acute myocardial infarction VT required and emergency treatment.

Various Drug, Synchronised D. C. Shock (Lown et al, 1967; De Sanctis, 1965) and artificial pacing (Sowton et al, 1964; Heiman and Helwig, 1966; and Moss et al, 1968) has been successfully used in the management of VT. List of the drugs that have been used in treatment of VT include (Cohen et al 1966) Atropine, Morphine, Magnesium, Papaverine, Chloroquine, Propranolol, Diphenylhydantoin, Antazoline, Bretylium (4), Quinidine, Procainamide and Lignocaine. Any treatment for VT in Acute myocardial infarct should be immediately effective and safe. Bretylium tosylate produce hypotension, parenteral propranolol might be hazardous when used in acute stage of myocardial infarct and its success rate is low (BMJ 1969; Usabiago 1967).

Of all these drugs only quinidine, procainamide and lignocaine are effective specific antiarrhythmic agents. Diphenylhydantoin and Bretylium may however be effectively used in certain cases resistant to lignocaine and procainamide.

Intravenous quinidine is very toxic. So procainamide and lignocaine has wider acceptance. Procaine amide (I.V.) is effective in 78% of the cases and if used in sufficient doses perhaps will be effective in higher percentage (Choen et al 1966). However it is more cardio-toxic can cause marked hypotension, dangerous widening of the QRS complex and even VF, and so require ECG and BP control for its administration. These complications except hypotension are however not very common (Friedberg 1959). Lignocaine is 4 to 5 times as potent as procaine amide, 100mg of it being comparable to 500mg of procaineamide (Cohen et al 1966), and as in therapeutic dosage it has no deleterious effect in the haemodynamic state of the patient it has a great advantage over other drugs in the management of the ventricular arrhythmias in acute myocardial infarction. But we found this drug effective only in 40% of the cases of VT. This high failure rate is perhaps due to not sufficient dose being used in some cases. The drug may perhaps prove more effective with some change in the policy of administration of this drug.

The effectiveness of the drug depends on its concentration in the plasma, and now there is some evidence that the drug given on the basis of weight has no practical bearing to the level of the drug in the plasma and is perhaps unnecessary to give this on weight basis (Scott et al 1968). So irrespective of the body weight a stat dose of 50mg lignocaine should be used. If this does not suppress the arrhythmia another 50mg should be repeated every 5

minutes till it is suppressed or a total dose of 200mg has been given or toxic symptoms develop. If the drug is effective, and infusion of it at 3 to 4mg per minute is setup. If on 4mg/mt should be made to decrease the rate to 3mg/mt over next 1-2 hours and then over next few hours to 2mg/mt, and over next 12 hours to 1mg/mt and then finally the drug is withdrawn. Any sudden increase in frequency of VPB or appearance of VT should be treated by a stat dose of 50mg, and if necessary by increase in rate of infusion. If the maximum stat dose of lignocaine is not effective in controlling the arrhythmia oral procainamide or other drug should be added in case of VPB, and in case of VT DC shock should be used immediately where available and I.V. procaine amide if not.

Synchronised DC Shock (Lown et al 1962) is effective and safe in 95 to 97% of the cases of VT (Lown, 1964; De Sanctis 1965). Perhaps it is the most effective method of treating VT but it is not readily available at all places and its administration require anaesthesia. Moreover many patients can be safely and easily converted with lignocaine, which is readily available, safe and easy to administer. But if the initial use of this drug is not effective no time should be lost in undertaking electrical conversion of the arrhythmia. It is not justifiable to administer depressant drugs to the point of toxicity when such an effective and safe method of therapy as electrical conversion is available. In case of moribond patients the therapy of choice is D.C. Shock and should be used immediately without anaesthesia. No time should be lost even to synchronise the shock and if VF does occur after unsynchronised shock it will revert promptly if another shock is administered immediately Cohen et al 1966. However lignocaine should be the drug of choice in case of VT due to digitalis or in digitalised patient, as there is some experimental evidence that D.C. Shock may be ineffective and may frequently induce VF or cardiac standstill in these circumstances Katz et al 1966; Lown et al 1965.

Contraindications to the use of lignocaine

Lignocaine is not effective in supraventricular arrhythmias, except atrial premature beats. And it could be dangerous in atrial flutter with blocks. 2:1 block may be converted to 1:1 conduction with marked increase in the ventricular rate (Hayes et al, 1967; Adamson & Spracklen, 1968). Similar effect has been reported also with the diphenhydantoin (Grissom et al, 1966) and quinidine and antazoline (Dreifus et al, 1964).

It also cause delay in conduction (Hilmi et al 1968; Spreacklen et al 1968). In unanaesthetised dogs with complete heart block it did not effect the atrial rate but slowed ventricular rate and caused prolonged asystole following abrupt cessation of ventricular drive (Hayes et al 1967) Special precaution should be taken in using this drug in patients with A-V block unless they are electrically paced.

Hepatic insufficiency will presumably increase the toxicity of lignocaine and so its presence is contraindication to its use (Soldon et al 1967).

Side Effects

De Clive-Lowe (1954) reported three cases of convulsion after an intravenous use of lignocaine at 12.5mg/minute. Dutton (1955) observed convulsion in another patient following

its use as pudendal block, (80ml of 1% solution). A personal experience of neuro-psychiatric symptoms following its use as local anesthesia was described by Bennet (1957). Goldman (1958) observed similar symptoms in an obstetric patient who received a total of 500mg lignocaine with hyaluronidase as pudendal nerve block. Foldes et al (1960) studied the toxic effect of 500ug/kg/min. of the drug given intravenously to ten healthy male volunteers. Dysarthria, disorientation, sweating, euphoria was noted in variable frequency. Muscular fasciculation was noted in all of them. Other symptoms recorded were: blurring of vision, diplopia, impaired perception of colour, sensation of cold or lump in the throat and heaviness in the chest. None of the subjects were able to tolerate the high infusion longer than 18mins. The average level of lignocaine in blood was 5.5ug/ml. Side effects varying from drowsiness, euphoria and lightheadedness, to loss of consciousness and even respiratory arrest which have precipitated cardiac arrest have been recorded after its use as an antiarrhythmic agent (Beydyseck et al 1966; Gianelly et al; Irossmaa et al 1967; Hayes et al 1967; Juwitt et al 1968; Julian et al; 1964). It appears the neuro-toxic effect of lignocaine depend on its concentration in the blood. Mild symptoms of toxicity occur at plasma level of 5mg/ml and more serious reactions at level above 10mg/ml (Foldes et al, 1960). But Jewitt et al (1968) noted twitching, confusion, and disorientation in two patients with blood level of 2.7 and 3ug/ml respectively. Gainelly et al (1967) observed stupor in three patients, two of whom had focal convulsion as well. Two of three patient were receiving lignocaine at 8g/min. and the third 3.5mg/mt. Blood levels of lignocaine were 22.8, 10.9 and 6.8mg/ml; respectively and the one with the lowest level of lignocaine developed convulsion. Thus there seems to be some lack of correlation between blood level and development of side effects. Similar lack of correlation between the blood level and duration of response of the drug as an antiarrhythmic agent has been noted before (Hayes et al 1967). This may perhaps be due to influence of some other 'individual' factor. Even the incidence of the side effect is noted in variable frequency by different observers. Killip (1967) who use higher rate of lignocaine infusion (4-5mg/mt), have given upto 6g. of the drug in 6 hrs period without observing convulsion. Lown (1967) saw petimal attack during lignocaine therapy but convulsion in only one elderly patient after repeated cardiac arrest and thought it difficult to distinguish between convulsion due to cerebral hypoxia and due to lignocaine. And Meltzer (1967) has not seen a seizure due to this drug. I have observed a higher incidence of the neurotoxic effect of the drug.

Side effect were noticed commonly at 4mg/mt. But whether while on 1mg/mt or 4mg/mt insignificant proportion of cases it occurred when the drip rate was temporarily and accidentally increased. This occurred some time while adjusting the drip set, or after withdrawal of blood for biochemical test from the same site and sometime due to other reasons like the drip being left to run faster accidentally after measurement of CVP, or the 'Flow Control' plastic clip of I.V. set becoming loose.

If the temporary increase in rate of infusion and hence the temporary increase in concentration of the drug in blood and hence in central nervous system is an important factor in occurrence of the side effect it could be remedied to a great extent just by use of

efficient metal clamps instead of the plastic one in the set; which gets loose very easily; by use of infusion pump for administration of the drug and perhaps by use of lesser strength of lignocaine.

However, if the use of the drug in wider scale beyond the close supervision of intensive care unit is contemplated it will perhaps be inevitable that even if the drug is used at 1 to 2mg/min, we might see more cases of neuro-toxic side effects. The exact nature of the CNS action of lignocaine is yet not clear. Some of the signs like muscular fasciculation and convulsion appear to be manifestation of cortical irritation; while others like drowsiness, and loss of consciousness due to cerebral depression. De Jon and Walts (1966) have proposed that most of the CNS manifestations of lignocaine—short of grand mal—seizure are attributable to seizure activity in the amygdala hippocampus complex. Perhaps lignocaine is mainly a cerebral depressant. The convulsant action of it may be due to preferential depression of inhibitory control normally exerted over excitatory input in cerebrum (De Jong et al, 1969). And the depressant effect of barbiturates and general anaesthesia and that of lignocaine on vital centres of the CNS may be additive (Gieddes and Questal, 19).

A therapeutically important but less well known CNS action of lignocaine group of drugs is their potent anticonvulsant property (Bernhard et al, 1955 & Bernhard & Bohm, 1965-15). Bernhard et al 1955 successfully used it to treat 10 cases of status epilepticus. They also noted that barbiturate and lignocaine have synergistic action on status epilepticus.

It thus appears the CNS action of lignocaine depending upon the concentration of the drug in the blood manifest as sedation (occasionally excitation) progress to anticonvulsant action, fine tremor, grand mal seizure and culminates in loss of consciousness (15).

Conclusion:— We have yet to have an ideal antiarrhythmic drug which is consistently effective, rapid in action and is safe and may be given by mouth. Lignocaine is fairly effective in management of the ventricular arrhythmia (except VF), and its effectiveness is comparable to that of procaine amide. Its main advantage is that it has less deleterious effect on the haemodynamic state of the patients and the rapidity of its action. But it has to be given intravenously and its effect is transitory so its use is limited to short term use only e. g. in the management of ventricular arrhythmia following cardiac catheterisation, angiocardiology or during and after cardiac surgery and Acute myocardial infarction.

Lignocaine is more neuro-toxic than procaine amide. The side effects are however short lasting, complete recovery in some within 5 to 10min. on temporarily discontinuing the drug. Some of the symptoms like heaviness over chest, loss of the consciousness etc may mimic the symptoms due to acute myocardial infarction and its complications. And if this is not appreciated the continued use of the drug may prove fatal. Moreover some of the neurotoxic effect like sudden arrest of respiration may precipitate cardiac arrest. The use of the drug still require careful supervision,

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