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PROPERTY OF NEOSTIGMINE AT THE TIME OF INDUCTION

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Introduction:

Waser[1] (1967) has used a minimal lethal dose of radioactive d-Tubocurarine(dtc) mixed with reversing dose of Neostigmine in the Mouse, taking autoradiographs from the diaphragm.

Although the animal survived, nevertheless there was no noticeable reduction in radioactivity at the level of diaphragmatic and plates when compared with the countrol group taking (dtc) alone.

He has concluded that Neostigmine does not displace (dtc) from the receptors and the restoration of diaphragmatic respiration must be due to the action of acetylcholine(Ach) on the other free receptors.

I have applied a modification of Waser's technique in man and I have been impressed by paramount safety and simplicity of this new method of anesthesia. Because of its unique clinical features we have found worthy to report it.

Material:

This work was carried out since November 1980 till now in Cancer Institute (University Hospital), and a pri-

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vate hospital.

Patients consisting of both sexes, having their age ranged betwen 5 to 79 years.

Almost all kind of surgeries have been included with the exception of open heart, neurosurgery and upper abdominal operations. The distribution of different surgery is summarized in table I.

Table 1

Operation Performed	No. of Cases
Abdominal Operation(Lower abdominal)	54
Laparatomy(inoperable)	15
Mastectomy(simple,radical)	26
Thyroidectomy and neck dissection	8
Tumor of head and face	40
Miscellaneous Tumor	28
Bronchial adenoma	1
Lumbar disc	18
Rhinoplasty	25
Plastic of breast and abdomen	4
E.N.T. Operations	52
Haemorrhoid	32
Lower limb fractures	40
Upper Limb fractures	21
Miscellaneous operations	68
	432

METHOD:

No premedication was prescribed, only a few apprehensive patients received 5 mg Diazepam IM.
On arrival to operating room the vital signs were checked and a sample of arterial blood taken for analysis,then, a teflon cannula was inserted IV and infusion was set up.

Anesthetic Method Consists of following steps, 0.4-0.5 mg d-tubocurarine(dtc) per/Kg is injected IV followed immediately by injection of 7-8 mg/Kg Thiopenton(5% solution), patients lungs are ventilated by pure 02 and Tracheal intubation is carried out,then,0.15-0.2 mg/Kg of morphine is given followed by IV injection of Neostigmine, 0.5 mg/Kg every 5 min.till the respiration is restored adequately (usually between 0.5 to 1.5 mg). Thereafter, anesthesia is maintained by inhalation of Halothan 1-1.5% and 02. The depth of relaxation is adjusted at the beginning of anesthesia by further dose of dtc (6-9 mg) but no more dtc is needed during anesthesia.
Atropine is administered only if the pulse rate becomes undesirably slow. Respiration usually starts by regular slow rhythm in 5-10 min and is adequate from the start.

Throughout the major operations, there is usually a good level of relaxation allowing the application of ventilator, whenever this is desirable. The abdominal wall retains a fair degree of relaxation. At the conclusion of long operations only 0- $\frac{1}{2}$ of usual dose of Neostigmine is enough for the reversal of curarization, given by titration as required. The patient wakes up smoothly, comfortably and painlessly with no delay.

RESULT:

This method of anesthesia has proved to be free of mortality and morbidity in the whole series. Patients were extremely satisfied by the prolonged analgesia and the lack of the sickness post-operatively.

Cardiovascular parameters remain in the normal range. The average blood gas analysis after the return of spontaneous respiration has been as follows:

PO_2 290 PCO_2 38 Ph 7.377

a mmHg, a mmHg,

Discussion:

This method of anesthesia possesses many beneficial properties. Some are considered individually below:

1- Maintenance of spontaneous respiration:

By return of effective diaphragmatic respiration the need for artificial ventilation is excluded. The respiration is a kind of deep, slow breathing providing adequate volume of gas exchange confirmed by repeated blood gas analysis and spirometry, the major question now is how Neostigmine restarts the diaphragmatic movement while the other body muscles are still deeply paralysed?

Based on the recent information this phenomenon can be explained as follows:

Neostigmine, even in 0.5 mg dose causes a prolonged and significant increase in acetylcholine (Ach)release from pre-junctional nerve ending (Riker 1969)[2]. This phenomenon causes some reduction in dtc receptor binding which is visible in diaphragmatic function. It has been known that Diaphragmatic muscle is the most reistant muscle in the presence of dtc and it requires 90% recepto-

rs occupancy to stop breathing (Paton 1967)[3]. Neostigmine together with higher rate of agoist impact reduces the rate of receptor occupancy and will restore the spontaneous breathing (receptor occupancy 90%)while, at this level of relaxation, the other body muscles are still deeply paralysed (receptor occupancy 70%). So, it is evident that 0.5 mg of Neostigmine causes approximately 10-15% reduction in receptor occupancy.

In an interesting case of bronchial adenoma,by application of this method, trachea has been widely opened for a period of 15 min. and tumor was easily removed with out the need for bronchial intubation.

2- Prolonged Muscle Relaxation:

By the use of this method, I have observed a fair degree of muscle relaxation throughout lengthy operation of 3-5 hrs., without the need for further dose of relaxant.

This blockade demonstrates the characteristic of a non-depolarising block as it is potentiated by a small dose of dtc and it is antagonized by administration of Neostigmine. It is difficult to explain the origin of this relaxation but probably many factors contribute to the establishment, i-e Dual block of receptors due to the prolonged contact with excessive concentration of (Ach) discharged by Neostigmine, exhaustion of Ach available stores after its initial release by Neostigmine (Blaber and Bowman 1963)[4]. and Halothan especial non-depolarizing property (Hughes and Payn 1970)[5].

3- Relief of Hypotension:

In daily practice of anesthesia the administration of dtc is always accompanied by some degree of hypoten-

sion, especially when halothane is added to anesthesia.

To explain this phenomenon many factors have been accused e.g. Histamin release, failure of venous return and CNS and ganglionic depression.

My experience indicates that the hypotension is mainly the result of Ach depression caused by dtc at the ganglionic level, and is easily reversed by administration of 0.5-0.1 mg of Neostigmine.

Although there is more bleeding from skin incision, which is preventable by the local use of Epinephrine, there will be less bleeding in the following stages of operation, due to slowing of the pulse rate combined with lower intra-thoracic pressure produced by slow and deep spontaneous respiration.

4- Potentiation of Analgesia:

Slaughter and all (1946)[6] reported twice analgesic action from Morphine when used in conjunction with Neostigmine. We have omitted the use of N20 in our anesthetic mixture and have never observed any objective sign of pain during operation.

This analgesia extends to the post-operative period and it is free from side-effect of vomiting, nausea and excessive mental depression.

This observation strongly suggests that the majority of post operative sicknesses might be due to the undue depression of cholinergic system.

Morphine eliminates tachpnea induced by halothane and the resultant slow, deep respiration is desirably adequate and this is confirmed by normal P_aCO_2 during procedure.

The mechanism of production of this potentiated ana-

lgesia is not clear as Neostigmine in contrast to physostigmine, does not cross the blood-brain barrier.

5- Anti-Shock Property:

This method is carried out in a few difficult cases of surgery producing enormous amount of bleeding and trauma and it has been impressive to find its excellent protection against shock state. The pulse rate and pressure and the blood pressure Remain stable and the extremities are pink and warm.

This anti-shock effect of Neostigmine is similar to alpha receptor blocker agents, except for its slow pulse rate.

6- Controle of Pulse Rate:

By administration of the appropriate amount of Atropine in this method one is able to control the pulse to a desirable rate.

In some febrile patient this method proved to be of value. We prefer to maintain a pulse rate of 70 beat per min.

This action is similar to the effect of Beta receptor blockers with the privilege of having an underpressed heart.

The use of Epinephrine to facilitate surgical procedures does not provoke acceleration of pulse rate dur to the antagonistic effect of Nestigmine with epinephrine. This is a major advantage during most of the plastic operations.

7- Safety:

Many potential hazards during general anesthesia is eliminated by achieving this method, e.g. emptied 02 cylinder, absence of electricity, Halothane over dosage,

and excessive hyper - hypoventilation etc.

The presence of bag movement is a valuable vital monitor, whenever there is no cardiac monitor at hand.

8- Economy:

N20 is omitted. There is no need for supplementing doeses of dtc and the reversing dose of Neostigmine can be reduced to half of usual doses. The ventilator apparatus is not necessary.

9- In Emergency Situation and Field Operation:

Due to its simplicity, safety, economy, this method promises to be most beneficial for emergency and field surgery. Even a single handed anesthesiologist would be able to manage anesthesia in 2 even 3 operating theatre simultaneously without needing a ventilator apparatus.

SUMMARY:

The use of a small dose of Neostigmine during induction of anesthesia provides many valudable clinical manifestation which have been discussed in detail. I believe this method of anesthesia might be desirable in emergency situations and whenever the ventilator is not available.

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