DISCUSSION
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Neuro-muscular relaxants constitute the sheetanchor in the technique of balanced anaesthesia. The qualities desirable in a good neuro-muscular relaxant are now fully established. It should produce brief non-cumulative, non-depolarizing neuro-muscular blockade with rapid onset and recovery. It should be easily reversible, and should be devoid of clinically undesirable cardiovascular side effects (such as, autonomic and haemodynamic side effects).

In an elderly patient all these qualities are the basic requirements, as they have diminished physiological reserves. Elderly patients have reduced ability to maintain homeostasis during stress, such as that of surgery and anaesthesia. These patients constitute a group at a higher risk. Pre-existing complications contribute further to this risk more so in the event of emergency situation.

In this clinical appraisal an effort is made to evaluate the risks of pancuronium bromide in elderly patients with pre-existing complications. No exact cut off age is defined for elderly age group and this range varies from 45 years upto 70 years (Ellison Norris, 1975). Elderly patient considered in this dissertation is an individual of chronological
age of 45 years and over, with the realization that
this may be at variance with true biological age of
the individual. Average age was calculated to be
56.8 years (Table-1) and average body weight was
43.8 Kg. (Table-3). It is evident that these elderly
patients with pre-existing complications (Table-7)
were mostly grouped under ASA grade III & III-E (Table-3).
Fifty patients in pancuronium group had 57 pre-existing
complications distributed amongst them.

MUSCLE RELAXANT PROPERTIES OF PANCRUORUM

(A) Onset of Action: It has a rapid onset of action.
Apaene was observed at $104.84\pm 5$ seconds & Neuromuscular
blockade as observed by twitch response, was complete
by $108.32$ seconds (Table -15). Any significant difference
between the onset of action with $0.08$ mg/Kg, dose &
$0.1$ mg/Kg was not found. In equipotent doses the onset
of action with tubocurarine was significantly longer
(Table-24).

Exact duration by which the onset of
action is complete is yet a controversy. Sellick (1956)
found onset of apnea by 45-90 seconds and Ehestola
(1977) observed this range as of 60-300 seconds. Norman
(1970) found 60% twitch depression at 270 seconds,
whereas Katz (1971) noted full depression of twitch
response by 297 seconds.
Results in this study are in accordance with the observations made by Dick (1970) & Lorhan and Lipmann (1972) who noted ventilatory depression by 2 minutes & complete muscle relaxation by 3 minutes.

Pancuronium therefore produces ideal conditions for an early intubation, significantly earlier than tubocurarine. It lacks the disadvantages of muscular fasciculations (which causes rise in serum potassium) as produced with use of succinylcholine. This is certainly an advantage in elderly patients with poor risk.

(b) Intubation time and conditions: With the use of 0.1 mg/kg, doses Intubations are possible at 193±14 seconds (3.2±.5 minutes). In equipotent doses the tubocurarine produces intubating conditions at 257±17 seconds, and this difference was statistically significant. Gallamine produced similar conditions by 204±34 seconds (Table -25).

These results are in accordance with those of Konarewicz (1971). He found Intubating conditions with pancuronium by 3 minutes, with Gallamine by 4 min. & with tubocurarine by 5 minutes. Other workers as Dobkin (1971) Füldes (1972), Joseph & Rockalli (1972), Lorhan & Lipmann (1972) & Fati et al (1979) had noted that intubations with pancuronium are possible between 2.5-3.5 minutes.
Intubating conditions were graded as Good in about 60% of cases, and all intubations were possible before 210 seconds. Galalumine produced good intubating conditions in 45% of cases (Table 25-9). Although these conditions are relative findings as they improve with time, yet it was distinct that tubocurarine could produce intubating conditions much later i.e. by 4-5 minutes. All the workers mentioned above had also noted good intubating conditions with pancuronium. The observations that Galalumine is equally good for Intubation is in accordance with those of Chandola et al (1979).

(c) Duration of action: The duration of action of pancuronium was observed by noting the return of spontaneous respiratory effort depended upon the initial dose. With the initial dose of 0.05 mg/kg, the average duration was found to be 37.2±5.75 minutes and with initial dose of 0.1 mg/kg it was 46.3±9.75 minutes. This difference was statistically significant (Table 25). Paco Florida & Trup (1971) and Felder (1972) had also observed that larger doses (as 0.1 mg/kg) administered for facilitation of intubations lead to longer duration of neuromuscular blockade.

Duration of spnana produced with pancuronium is also a controversy. Lohan & Lippa (1972).
Kawabara (1971), Stengert et al (1971), Pace Florida & Trop (1971) found it as of the range from 65 up to 90 minutes. In most of these trials potentiating drugs as Halothane or nesu-leptanalgesic are used. Others have used Dizepam, Ketamine & methoxyflurane during anaesthesia. Even succinonium has a disputed role, as (Katz 1971-b) noted that it potentiates pancuronium blockade & Krutina & Makalainen (1977) found just the contrary results.

It was observed in this study that pancuronium produces an intermediate duration of blockade, whereas in equipotent doses Gallamine has a shorter duration of action and Tubocurarine causes a blockade of significantly longer duration (Table-25). Apnoea duration produced with tubocurarine is in accordance to those found by Pandit & Dundes (1971) and Bennett (1972). The apnoea duration observed in present study due to pancuronium (when use of potentiating anaesthetic drugs was avoided) is comparable with results of other workers as, Sellicks (1966), Varma & Sharma (1970), Talivaa (1971), Feldes (1972), Nana et al (1972), Bhargava and Chatterjee (1977), Vickers (1973) & Chandela (1979). These workers have observed apnoea duration in the range of 30-60 minutes. No potentiation of nerve-muscular blockade was observed with prior used of succinonium in this trial.

Dechene et al (1972) had observed that major
dependent on body weight, dose & age. In this trial where age was a limiting factor (i.e., all patients were elderly), the other two factors such as dose administered in relation with body weight, were definitely in relation to apnoea duration. 0.1 mg/Kg. doses produced apnoea of significantly longer duration than produced by 0.08 mg/Kg. doses (Table 17 & 18).

Mean duration of apnoea with pentamidine in elderly patients for emergency surgical intervention was 46 ± 10.35 minutes. It was significantly longer than the apnoea produced by 0.08 mg/Kg. doses in patients for elective surgery (Table 17). The patients undergoing emergency surgery were those, mainly with Intestinal obstruction and their ASA grade were ASA III– E or IV–E. They had low general condition, shock, dehydration & electrolyte imbalance. These pre-existing complications were perhaps contributory to this significant difference between apnoea in patients with Intestinal obstructions & apnoea in elective surgery patients. It was similarly observed by Sallick (1982) & Moroto (1973) who had also noted that apnoea duration may be prolonged in patients of Intestinal obstructions with electrolyte imbalance.

Repitition of supplementary doses was done at the end of apnoea & due to incomplete relaxation. etc. The doses used were mostly 1–2 mg. I.V. Their requirement was minimum between 30–60 minutes when 0.08 mg/Kg.
Obviously it again proves that apnoea is dose dependent in case of pancuronium.

1) **Reversal of blockade:** Average duration of anaesthesia lasted 95–12 minutes (Table-4). Reversal of neuro-muscular blockade was attempted in the presence of spontaneous respiration. Mean duration of spontaneous respiration was noted as 17 minutes (Table-20) & then injection of Neostigmine 2.5 mg with 1.2 mg Atropine was administered. Reversal was graded as easy or difficult at 5 minutes of end of this injection (McDowell & Clarke, 1969).

Reversal of neuro-muscular blockade was found to be easy in almost all the cases (96%) irrespective of ASA grades. Two cases of difficult reversal were noted. (Table-20). One patient of ASA grade II had complete reversal at 10 minutes, She had developed arrhythmia intra-operatively and marked bradycardia was (Table-22) observed at reversal. Cause perhaps was hyperkalaemia, & Vagal stimulation. Arrhythmia had responded post-operatively to injection calcium and injection atropine under EKG monitoring. This association of arrhythmia, & bradycardia with reversal of blockade was also noted by Feldes (1972), Ostheimer (1977) & Osma (1978-8).

In the other case of emergency exploration for acute intestinal obstruction the reversal was delayed upto 15 minutes. When administration of 3 mg of
Neostigmine had completely reversed the blockade. Cause of delayed reversal time was perhaps the associated electrolyte & acid base imbalance together with low general condition. Mereto (1973) observed similar situations in his trial. Difficult reversal was also observed by Monks (1972), Castleden (1975), McLeod (1979), Babtsky (1974) has reported of a case of prolonged blockade without any detectable obvious cause.

Excluding these two cases of difficult reversal out of total 50 patients under trial in all the remaining cases reversal was easy. This is fairly in accordance to the results of McDowell & Clarke (1969), Baird (1970), Pace Florida & Trop (1971), Fogdall & Miller (1973), DeAngelis (1974) & Ramargupta (1980).

Reversal of other two relaxants was also found to be easy in all cases. It is to be noted however that number of cases under these groups were small as compared to pancuronium group, and that these were not used in emergency cases (Table -27).

It is thus concluded that reversal of neuromuscular blockade of pancuronium was easy in most of the cases & no event of prolonged apnoea or recurreriration was observed post-operatively (Table-22).
CARDIOVASCULAR EFFECTS, INTRA & POST-OPERATIVE EVENTS

IN RELATION WITH PRE-EXISTING COMPLICATIONS IN ELDERLY.

Cardiovascular dynamics was observed continuously in both intra and post-operative periods.

Pancuronium provided marked cardiovascular stability in most of elderly patients. These were patients undergoing major surgical procedures (some lasting over 240 minutes) with marked loss of blood, elderly patients for emergency surgical intervention (with low general condition, shock, dehydration, electrolyte imbalance) and other patients with various pre-existing complications.

A definite rise in pulse & mean arterial blood pressure was also noted in some cases. Significant rise in pulse was observed in patients of ASA grade III, and in twelve patients where 0.1 mg/Kg doses were used as initial doses for intubations (Graph I 4II).

This rise in pulse rate is related to sympathomimetic & vagolytic actions of pancuronium as observed by Zsigmond (1974), Tomilson (1979) & Reinhoff (1980).

Significant rise in pulse rate was noted by Fedde (1971), Helms & Kennedy (1971). Similarly other workers as Labbe & Deenen (1971), Steckling (1972), Joseph & Bechalli (1972) & Ehrismann and Chatterjee(1972)
had also observed this rise.

Gallamine in equipotent doses caused a highly significant rise in pulse, of 21% in relation with pre-induction values (Graph II-a). Also the tachycardia produced with gallamine was significantly more as compared to pancuronium. (Table-29).

In emergency cases, where mean pulse rate (pre-induction values) was over 110/min, the pulse rate stability was marked (Graph I-a). Konessaroff (1970), Levin & Dillion (1972), Lyons & Clarke (1975) & Chandola et al (1973) have all found minimum changes in pulse rate with use of pancuronium.

Mean arterial blood pressure (MAP) changes were observed mainly in the patients where 0.1 mg/Kg. doses were used & in emergency group of patients. In both of these groups the rise was significant but gallamine caused even more marked & significant rise. Tubocurarine had caused a highly significant fall in MAP during its use (Graph I-b & II-b).

Rise in MAP was also observed by Konessaroff (1970), Kalman & Kennedy (1971), Stoelting (1972), Bennett (1972), Bhargava & Chatterjee (1973) and Chandola et al (1979).

There was no significant change in MAP in 31 patients (62%) under pancuronium group, which comprised
of elderly patients with pre-existing complications such as hypertension, angina pectoris, irregular pulse, mitral valve disease, chronic obstructive pulmonary diseases, renal diseases such as hypernephroma and thyroid disorders. Even in major surgeries lasting over 240 minutes of anaesthesia duration the MAP changes were remarkably minimal. These results are in accordance with those observed by Sellick (1968), Saxena & Bonta (1971), Speight and Avery (1972), Foldes (1972), Lorhan & Lippmann (1972), Lyons & Clarke (1973), Gratama & Makaleinen (1977), Pati et al (1979) and Pramila Vora (1980).

It is possible that the rise in MAP and pulse rate with pancuronium are partially also due to the residual effects of Intubation reactions. And therefore the significant results observed relative to pre-induction values may be a result of both (residual effects of Intubation reactions & positive ionotropism of pancuronium).

But a definite decline in both MAP and pulse rate after 6-8 minutes of Intubations is seen (Graph I & II). The cardiovascular effects of non-depolarizer relaxants including pancuronium appear by 6-10 minutes of their administration, and are sustained in most cases upto 30-40 minutes.
Shanks (1979) observed a definite correlation of apnoea & plasma level of pancuronium. It is also a known fact that rise in pulse & MAP are because of its vagolytic and sympathomimetic effects. (Templon, 1979, Fokinoff, 1980). Thus, a relationship is evident between the plasma levels of pancuronium, duration of apnoea & duration of cardiovascular effects. It is similar to the observations of this study, that cardiovascular effects are mostly noted up to 30 minutes, apnoea duration observed is 37 minutes. Both of these are related to plasma levels of pancuronium. Agoston et al (1973) has found that 60% of pancuronium in plasma disappears by 30 minutes. Verma & Sharma (1971) and Speight & Avery (1972) had noted cardiovascular effects up to 30 minutes. Hence it is concluded on the basis of observations in the present study that cardiovascular effects are seen mostly up to 30 minutes, and that these are definitely in relation to plasma levels of the drug & duration of apnoea.

Hypertension or rise in MAP beyond 20 mm Hg (above pre-induction values) was observed with use of pancuronium in 4 cases (Table -21). Two patients were pre-operatively diagnosed as hypertensives and were under antihypertensive therapy such as reserpine derivatives. Two other cases (are each of ASA II & III grades) without pre-existing cardiovascular complication had
had rise in MAP beyond 20 mm Hg.

This marked rise could perhaps be due to positive ionotropism (Birchard, 1973), raised levels of sympathomimetics (Eckinoff, 1930 and Tomilson, 1979). Precipitation of hypertension was observed by Lorhan and Lippemann (1972) & Freley (1973). Rise in MAP was also observed by Asari & Takahashi (1973) when pento- 
scine is used with pancuronium.

Hypotension or fall in MAP more than 20 mm Hg (Below pre-induction values) was observed in five cases in pancuronium group (Table -29). Incidentally all of these five elderly patients had marked blood loss due to prolonged surgical procedures. In a case of nephrectomy the MAP was stable (+10 mm in relation to pre-induction values) upto 180 minutes & later hypotension occurred when bleeding was marked. Similarly in another case of, Smith -patterson nailing & plating for fracture of femur neck, had hypotension after 70 minutes of stable MAP. Other cases were resection of fibro- 
sarcoma, ovarian tumour & panhysterectomy. It is noteworthy that in most of other major surgeries, at least nine of which were of 2.5 -4 hours duration, the hypo- 
tension was still not observed.

In contrast to it tubocurarine caused hypotension in 40% of the cases. The difference between it’s incidence with pancuronium & tubocurarine, was
associated more with histamine release as was found by McDowell & Clarke (1969), Stewart & Lund (1970), Stealting (1972) and Joseph & Bockalli (1972).

In one case arrhythmia was observed with use of pancuronium (Table-22). The cause was association of hyperkalaemia, respiratory acidosis & vagal stimulation. Similar association is noted by Foldes (1972), Owens (1973-b) and Osthheimer (1977). Brichard (1973) had noted the increased incidence of arrhythmia in presence of respiratory acidosis. It is also observed that whereas in slight acidosis sympathetic system is predominant, greater degree of acidosis causes definitely increased sensitivity to vagal stimulation. In this patient the muscarinic effects of Neostigmine were marked but it still responded to atropine.

Bradycardia was observed in some other cases also, after reversal with 2.5 mg Neostigmine, Inspite of pre-administration of 1.2 mg of atropine the bradycardia was found. It however responded to repetition of atropine. Thus this complication i.e. bradycardia in 8% cases was due to muscarinic actions of Neostigmine (Table-22).

Pre-existing respiratory compli-
ations in elderly patients would most likely be
associated with intra-operative bronchospasm & hypotension (Levin et al., 1971 and Freeman, 1976). In the present appraisal among elderly patients with pre-existing respiratory complications such as chronic obstructive pulmonary disease, diabetes, chronic bronchitis, emphysema, and bronchial asthma, intra-operative hypotension & bronchospasm was not observed & post-operative respiratory insufficiency was nil. Rise in MAP was found in 2 cases of chronic bronchitis but in none of cases with emphysema.

A case of emphysema thoracis for thoracotomy and decortication pleura had uneventful course in both intra & post-operative periods.

Histamine release was not observed in three cases of bronchial asthma. A case of eosinophilia, no event of bronchospasm, cyanosis, erythema, hypotension was observed in these cases. Stejnov (1969), Levin & Dillen (1972), Leshan & Lippmann (1972) & Light et al. (1975) have also not observed any incidence of histamine release. However, Buckland & Avery (1973) and Krauz and Anathanarayan (1978) had noted significant histamine release with procainurea.

Tubocurarine did cause hypotension in a case of bronchial asthma for prostatectomy. It's use was also associated with hypotension in four patients of chronic bronchitis & one of

Light et al (1973) observed that the patients with adult respiratory distress syndrome are ventilated better with use of pancuronium.

Patients with renal diseases & genitourinary complications are mostly associated with anaemia, hypovolaemia & uremia (Kanvyasi et al, 1972 and Popescu, 1972). These cases are potentially risk cases where excretion is prolonged and hence rescurarization may occur (Munks, 1972; Castleden, 1975; McLeod, 1975 and McLeod, 1979).

In the present study which constituted of elderly patients with pre-existing renal diseases such as, malignancy, hydronephrosis, non-functioning unilateral kidney, renal pelvis stones, and genitourinary complications such as enlarged prostate, urinary tract infections, raised serum urea levels. Intra-operatively in most of these cases no complications such as hypotension, hypertension, or prolonged anaesthesia was observed. Also no event of rescurarization was noted. Absence of these intra-
operative & post-operative complication in patients of renal diseases with use of pancuronium was also observed by Kamvyssi et al (1972), Popescu (1972) & Bevan (1981).

In a patient with marked obesity, rise in MAP beyond 20 mm Hg was observed. In another obese patient for cholecystectomy due to gall stones the variations in MAP & pulse rate were minimal.

No event of resistance to pancuronium or its increased requirements were observed in two cases for cholecystectomies as was found earlier by Varna & Sharma (1971) and Nana et al (1972). In the present study pancuronium was used in eleven anaemic patients, who are according to Knass (1977) mostly associated with intra-operative tachycardia and hypotension. Only one out of these eleven patients had intra-operative hypotension & tachycardia (that even because of associated surgical trauma and bleeding). On the contrary tubocurarine was associated with hypotension in 3 out of 6 anaemic patients.

Stability of cardiovascular dynamics with pancuronium in anaemia & hypovolemia was also observed by Dobkin (1971), Kamvyssi et al (1972), Chasakis (1972) &
Lowhan & Lippman (1972).

A remarkable case of stable intra-operative dynamics was observed in a patient of thyrotoxicosis (basal pulse rate 106/minute). Who had history of coma 10 days prior to surgery because of cerebral malaria, and was under treatment with antithyroids. He underwent uneventful thyroidectomy with total of 12 mg. of pancuronium. MAP and pulse rate variation was nil, operation lasted 3½ hours.

Pancuronium provided marked cardiovascular stability in prolonged, major surgeries for resection of malignancies. Also, worth mentioning is the group comparing up of patients for emergency surgeries. These elderly patients with pre-existing hypovolemia, shock, electrolyte imbalance, tachycardia had minimum intra- & post-operative complications (Table -21, 22).

One post-operative death was observed in an emergency case of intestinal perforation with gangrene. This patient died of tachycardia & shock on 2nd post operative day. This death was not attributable to use of pancuronium as intra-operative & post-operative periods were uneventful. (Table-22) and reversal was complete.