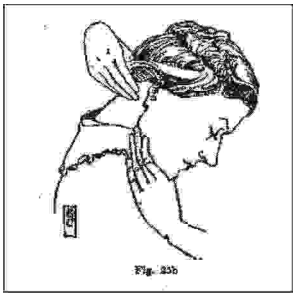
ORIGINAL PROF-1164

TREATMENT OF TETANUS;
THE USE OF CONTINUOUS ATROPINE SULPHATE INFUSION



DR. SAJID SHEIKH, MBBS, FCPS
Associate Professor of Surgery
Punjab Medical College
Faisalabad

DR. A.G. REHAN
Principal/Professor Of Surgery
Punjab Medical College
Faisalabad

DR. MOHAMMAD AJMAL , MBBS, FCPS
Senior Registrar
S-IV, DHQ, Hospital
Faisalabad.

Dr. Muhammad Yousaf Shah
Professor of Surgery
Punjab Medical College
Faisalabad

ABSTRACT… Objective: (1) To find out the result of drug to what extent it reduces the need for sedatives. (2) To compare the results with other treatment. **Study Design:** Prospective analytical. **Setting:** Tetanus ward D.H.Q. Hospital Faisalabad/ **Subjects & Methods:** Six patients with Tetanus were studied **Inclusion Criteria:** Adult male&females suffering from Tetanus. **Exclusion Criteria:** Patient with known peptic ulcer disease and benign prostatic hyperplasia. **Results:** Six patients were given trial of Atropine infusions with continuous monitoring of pulse and blood pressure. Patients were provided conventional sedation along with Atropine infusion. The requirement of sedative drug was significantly reduced when the dose of Atropine was gradually increased. The patients remained mentally alert with marked reduction in muscle spasm, convulsion ,no element of anxiety or agitation. Respiratory problems were minimized. One female expired probably due to septic shock from induced abortion. **Conclusion:** Atropine sulphate is cheaper drug ,easily available ,short half life, minimal side effect and much important in developing and under developed countries where ICU facilities are not available.

INTRODUCTION

Tetanus is a disease of 3rd world with high mortality in Pakistan (40.6%)[1], with almost complete control in free world only 50 cases a year in U.S.A[2]. Our tetanus ward receives about 60 cases/year mostly from near and periphery of Faisalabad. The effective control of disease in developed nations is due to tight vaccination and availability of I.C.U. and high dependency units which is still a dream in our country. It is true to say that tetanus is a third world disease which requires Ist world technology in the form of ventilatory support and I.C.U. coverage[3]. Disparate therapies have been tried focusing on fatal spasm which are major symptoms.

Muscular rigidity and spasms of the chest wall, diaphragm & abdomen lead to restrictive defects. Pharyngeal and laryngeal spasms produce respiratory failure or life threatening airway obstruction. Poor cough

from rigidity, spasm and sedation lead to atelactasis and risk of pneumonia is high. The saliva is not swallowed copiously, the profuse bronchial secretions, pharyngeal spasm and raised intrabdominal pressure and gastric stasis all increase the risk of aspiration.

Ventilation/Perfusion mismatching is also common. Consequently hypoxia is a uniform finding in moderate or severe tetanus even when chest is radiologically clear. The mainstay of treatment in controlling rigidity & spasm is sedation with Benzodiazepenes. Benzodiazepene augment GABA agonism, by inhibiting an endogenous inhibitor at GABA-A receptor. Diazepam is given by various routes is widely used. Doses as high as 100mg/hr have been reported, but long acting metabolites (oxazepam and desmethyldiazepam) may lead to accumulation and prolonged coma.

Additional sedation is provided by Phenobarbitone (which further enhances GABA ergic activity) and other drug is chlorpromazine. Propofol has been used for sedation with rapid recovery on stopping infusion. The above mentioned three drug combination is widely used in our setup.

Sudden death is a feature of severe tetanus. The cause remain unclear. Probable explanation include a loss of sympathetic tone, catecholamines induced cardiac damage and parasympathetic tones and storms. The control of autonomic dysfunction is significant in management of tetanus. Magnesium Sulphate infusion is an alternative for ventilatory support where such facilities are lacking[4].

A trial is done already in our unit regarding the use of magnesium sulfate infusion for control of autonomic cardiovascular instability.(sympathetic over activity)[5].

It was found more effective in stage 1 and 2 tetanus specially with labile hypertension. Very little has been known about parasympathetic over activity involvement in tetanus.

DISCUSSION

Tetanus is an infection due to bacillus of clostridium Tetani, the clinical picture is result of intoxication caused by toxin of this bacillus. The tetanospasmin released by mature bacilli is distributed by lymphatics and vascular circulation to end plates of all the nerves .Tetanospasmin then enters the nervous system peripherally at the myoneural junction and transported into the neurons of CNS.

These neurons become incapable of neurotransmitter release. The neurons which release GABA and glycine, the major inhibitory neurotransmitter, are particularly sensitive to tetanospasmin leading to failure of motor reflexes Responses to sensory stimulation resulting in generalized contraction of agonist and antagonist musculature characteristic of tetanic spasm.

Since 1938,many authors reported that tetanus toxin inhibits Acetylecholinesterase (ACHE) and from that point of view it resembles with organophosphorus compounds[6].

The addition of oxymes, ACHE restoring agents in the treatment of tetanus is based on this principle. The motor neuron over activity releases Ach on the other hand in experimental tetanus not only are synthesis, storage and liberation of ach in sensitive organs augmented but also tetanus toxin itself has a cholinergic action. All these are in turn the cause of parasympathetic overactivity, broncho-spasm, bronchial hyper secretion, hyper salivation, profuse sweating (seen in clinical picture) are all muscarinic signs of Ach. Although magnesium sulfate is said to suppress Ach at the ganglia and vagal nerve terminal[7]. Our trial in this unit showed that excessive salivation and bronchial secretions were not suppressed by magnesium. It is known that early in the course Ach stimulates nicotinic recepters at sympathetic ganglia and cause tachycardia and mild hypertension ,later it stimulates muscarinic receptors or blocks ganglionic transmission by hyper-polarization resulting in bradycardia and hypotension. In the presence of excessive accumulation of Ach in adrenal gland as well as in muscles as seen in severe organophosphorus

intoxication ,nicotinic action may mask some of muscarinic effects .

Thus tachycardia may result from stimulation of sympathetic ganglia to overcome the usual bradycardia due to muscarinic action on the heart. Therefore the appearance of fasciculations and specially slow and progressive increase of heart rate on ECG are the signals to increase the atropine infusion rate until the symptoms had disappeared and heart rate has become normal.

RESULTS

In our study six patients; 4 males and 2 females, average age between 25 to 60 years were studied. 2 males presented with road traffic accident injuries out of remaining 2 males one presented with no evidence of injury (forgotten trauma.) the other patient presented with local tetanus of left forearm (after ORIF).

Patient-I. Local tetanus			
Day	Atropine	Diazepam	Phenobarbitone
1	50MG	20MG	300MG
2	100MG	20MG	300MG
3	200MG	10MG	NIL
4	250MG	10MG	NIL
5	500MG	05MG	NIL
6	400MG	NIL	NIL
7	400MG	NIL	NIL
Total	1900MG	60MG	600MG
Avg/Day	171.4MG	8.5MG	85.4MG

Out of 2 females 1 female got tetanus after induced (septic abortion). The other developed tetanus from household injury. All the patients were sedated in the form of inj. Diazepam 10mg/2ml.inj.phenobarbitone 200mg/2ml and inj. largactil 50mg /ml. Out of six patients ,one female patient expired probably due to septic shock from induced abortion. The best response was seen in patient with local tetanus in which minimum dose of atropine was given with minimal sedation.

Patient-II. Forgotten Trauma			
Day	Atropine	Diazepam	Phenobarbitone
1	250MG	60MG	300MG
2	500MG	60MG	200MG
3	1000MG	30MG	200MG
4	1500MG	20MG	100MG
5	2000MG	10MG	50MG
6	2000MG	10MG	NIL
7	2500MG	05MG	NIL
8	2500MG	05MG	NIL
9	3000MG	05MG	NIL
10	2500MG	10MG	NIL
11	3000MG	05MG	NIL
12	3500MG	05MG	NIL
13	3500MG	05MG	NIL
14	3000MG	05MG	NIL
15	2500MG	05MG	NIL
16	2000MG	05MG	NIL
17	1500MG	05MG	NIL
18	2000MG	05MG	NIL
19	1500MG	NIL	NIL
20	1000MG	NIL	NIL
Total	41250MG	2500MG	550MG
Avg/Day	2062.05MG	12.5MG	27.5MG

This patient had shortest stay, most probably due to best prognosis in local tetanus. Shortest incubation period was observed in RTA injuries, in all of the patients tracheostomy was performed. Accumulation of ACh in CNS is believed to be responsible for the tension ,

anxiety and restlessness of the patient. All the patients were found alert with out tension and no agitation was observed, it all helped in better nursing care and treatment.

Patient-III. House hold injuries				
Day	Atropine	Diazepam	Phenob-arbitone	Largectil
1	1500MG	20MG	300MG	100MG
2	1500MG	20MG	300MG	100MG
3	2000MG	30MG	300MG	50MG
4	2500MG	20MG	200MG	50MG
5	2500MG	20MG	200MG	50MG
6	3000MG	10MG	200MG	50MG
7	2500MG	10MG	N10MG	50MG
8	3000MG	10MG	NIL	NIL
9	3000MG	10MG	NIL	NIL
10	3000MG	05MG	NIL	NIL
11	2000MG	05MG	NIL	NIL
12	3500MG	05MG	NIL	NIL
13	4000MG	05MG	NIL	NIL
14	3500MG	NIL	NIL	NIL
15	2500MG	NIL	NIL	NIL
16	2000MG	NIL	NIL	NIL
17	1500MG	10MG	NIL	NIL
18	1000MG	10MG	NIL	NIL
19	1000MG	05MG	NIL	NIL
20	500MG	05MG	NIL	NIL
21	800MG	05MG	NIL	NIL
Total	46800MG	205MG	1500MG	450MG
Avg/Day	2228.5MG	9.76MG	71.4MG	21.4MG

The patients had no respiratory complaints and no aspiration pneumonia. Initially flushing was observed in all patients on Atropine infusions which gradually subsided.

Patient-IV. Forgotten Trauma				
Day	Atropine	Diazepam	Phenob a-rbitone	Largectil
1	800MG	30MG	600MG	400MG
2	800MG	30MG	400MG	300MG
3	1000MG	30MG	300MG	300MG
4	1500MG	20MG	300MG	200MG
5	1500MG	20MG	200MG	100MG
6	1000MG	20MG	200MG	100MG
7	800MG	15MG	200MG	100MG
8	700MG	10MG	200MG	50MG
9	1000MG	10MG	100MG	50MG
10	1500MG	10MG	200MG	NIL
11	1500MG	05MG	NIL	NIL
12	2500MG	05MG	NIL	NIL
13	2500MG	05MG	NIL	NIL
14	3000MG	05MG	NIL	NIL
15	3000MG	10MG	NIL	NIL
16	3500MG	05MG	NIL	NIL
17	3000MG	05MG	NIL	NIL
18	2500MG	05MG	NIL	NIL
19	1500MG	NIL	NIL	NIL
20	500MG	NIL	NIL	NIL
Total	32600MG	230MG	2900MG	1600MG
Avg/Day	1630MG	11.5MG	145MG	80MG

The patients were febrile in the beginning but later on the temperature was found normal. Nebulization was provided to each patient to prevent dryness of tracheal mucosa. Patient No 2 got atrial fibrillation on 7th day witch disappeared early. Patient 3 and 4 got complaint of hematuria which spontaneously resolved, other renal

function were found normal.

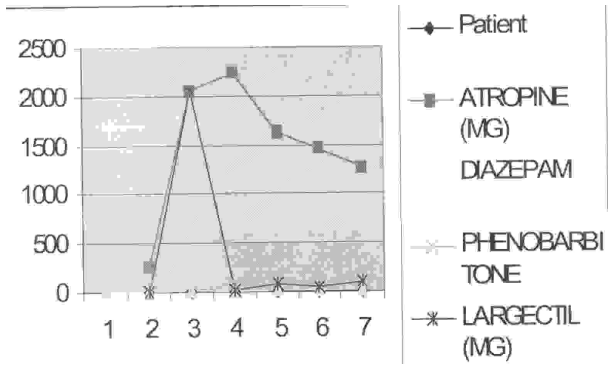
Patient-V. RTA Injury				
Day	Atropine	Diazepam	Phenob a-rbitone	Largectil
1	500MG	30MG	300MG	200MG
2	800MG	30MG	300MG	150MG
3	800MG	30MG	300MG	100MG
4	1000MG	20MG	NIL	50MG
5	1000MG	20MG	NIL	50MG
6	2000MG	10MG	NIL	NIL
7	3000MG	05MG	NIL	NIL
8	3500MG	05MG	NIL	NIL
9	3000MG	05MG	NIL	NIL
10	2000MG	05MG	NIL	NIL
11	1000MG	05MG	NIL	NIL
12	1000MG	NIL	NIL	NIL
13	500MG	NIL	NIL	NIL
14	500MG	NIL	NIL	NIL
Total	20600MG	165MG	900MG	550MG
Avg/Day	1471.4MG	11.7MG	64.2MG	39.2MG

It is proved that the use of continuous Atropine infusion markedly decreases the use of sedatives without aggravating respiratory failure and prevents from coma due to excessive use of sedatives.

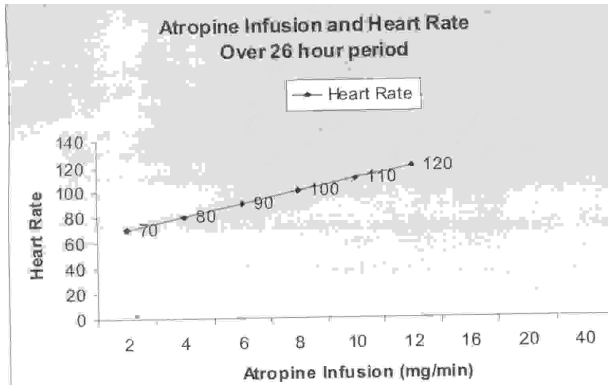
This was a fist trial in our country and second after D. Dolar[8]. Further trial is needed in our country and there is a need that it must be compared with ventilatory support along with minimal use of muscle relaxants on ventilators in the form of Atropine infusion.

Patient-VI. RTA Injury				
Day	Atropine	Diazepam	Phenob a-rbitone	Largectil
1	1000MG	20MG	600MG	300MG
2	1500MG	20MG	300MG	200MG
3	1500MG	15MG	200MG	150MG
4	2000MG	10MG	200MG	100MG
5	1500MG	10MG	100MG	50MG
6	1000MG	05MG	100MG	50MG
7	800MG	05MG	NIL	NIL
8	800MG	05MG	NIL	NIL
Total	10100MG	90MG	1500MG	850MG
Avg/Day	1262.5MG	11.2MG	187.5MG	106.2MG

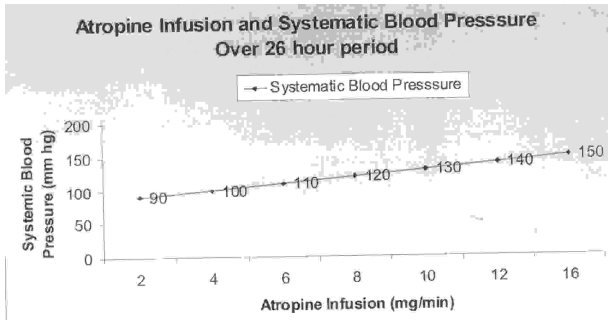
Average patient data				
Sr.No.	Inj. Atropine	Diazepam (mg)	Phenoba-rbitone (mg)	Largectil (mg)
1	271.42	8.5	85.4	0
2	2062.05	12.5	27.5	2062.05
3	2228.5	9.76	71.4	21.4MG
4	1630	11.5	145	80MG
5	1471.4	11.7	64.2	39.2MG
6	1262.5	11.2	187.5	106.2MG
Average dosage of drugs given to 6 patients				



Drug dose response relationship in 6 patients



Relationship of heart rate with atropine



Effect of atropine on blood pressure in 6 patients

REFERENCES

1. Raza S.N., Hussein I, Amjad M, Shah AA, **Prognostic factors in adult tetanus** J post Grade med Ins 1997 , 8 (3,4) 64-7.

2. Ajmal Khan, Javed Iqbal, Abdul Rashid, **Identification of Pathogenic and prognostic high risk factors in tetanus; One year experience.** The Professional Vol. 10,No.03 Jul, Aug, Sep, 2003(172-74).

3. Delport SD Neonatal tetanus. **An opportunity for prevention.** South African Medical J 1990 77;78-9.

4. Hollao VM, Clork GM(1975) **Autonomic manifestation of tetanus.** Anaeth Intensive care 3:124-147.

5. Ajmal khan, Javed Iqbal, Abdul Rashid, **Magnesium sulphate infusion: A novel approach in treatment of tetanus.** The Professional Vol: 10.NO.04, OCT, NOV, DEC, 2003.

6. Leonardi G Nair KG, Dastur FO, Kamat JS, Desai Bt (1973) **Evaluation of Cholinestrase restoring agents in the treatment of tetanus in man.** Jinfeet Dis 128:652-657.

7. Murphy SD (1975) pesticides In: Casasete LJ, Doull J(eds) **toxicology the basic science of poisons.** Mac Millan, New York Toronto London pp. 408-453.

8. Dolar D. **The use of continuous atropine infusion in the management of the severe tetanus** Inten Care Med 1992;18:26-31.