Analyzing the Effects of Dexamethasone Injection in Reduction of Mortality and Pathologic Effects Caused by Organophosphate Poisoning on rat-s lung

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Organophosphate compounds have been used as Pesticides in agriculture from a long time ago. The most common cause of death by these compounds is the related pulmonary complications. Since there have seen no study about the effects of dexamethasone on the reduction of mortality caused by Organophosphate poisoning and its pathologic effects on lungs, we decided to study this matter. This research was done on rats. 40 rats were randomly divided into two groups of control and treatment. Both groups were injected 25 mg/kg of Dichlorvos poison subcutaneously. The control group was injected 0.5 ml of physiological Saline and the treatment group was injected 100 mg/kg dexamethasone intraperitoneally. Then the rats of each group were analyzed separately for the rate of mortality and apnea. The lungs of the sample rats were sent to pathologic unit for further analyzing. The information was analyzed using spss 17 and chi square statistic test. Significant level was considered 0.05. In treatment group 10 rats (50%) survived while in control group all the rats were died which shows that the mortality was significantly higher in control group (p Value = 0.033). The average time period to mortality was also significantly higher in control group. The results had a significant difference in first class vascular congestion (p Value = 0.007) and second class hemorrhage (p value = 0.046) between the two sample groups. As a general conclusion it seems that dexamethasone can somehow reduce the destructive effects of Organophosphate poisons in alveoli and reduce the mortality significantly.

Key words: Dexamethasone, Organophosphate poisons, rats, death rate, pathologic effects.

Organophosphate compounds have been used as pesticides in agriculture and also in chemical weapons. The most common cause of hospitalization due to pesticide poisoning is for being in contact with Organophosphate poisons (above 80% of the cases). 3 million individuals are being poisoned with these poisons annually and 250 thousand of them die¹.

The death because of Organophosphate poisons is multifactorial but the main reason is pulmonary complications. Organophosphate compounds inhibit the Cholinesterase enzyme and result in aggregation of Acetylcholine on the surface of neural-muscular receptors, so their effects are appeared². The most common manifestations of Organophosphate poisoning are: hyper-salivation, increase of pulmonary...
mucus, running nose, diarrhea, incontinence of urine, bronchial spasm, vomiting and myosis. Extra-aggregation of mucus in airways and in pulmonary alveoli is one of the main reasons of mortality in these patients³.

Despite the enormous progresses made in medical science, treatment of Organophosphate poisoning haven’t changed in the last 50 years and it mainly includes Atropine, Oximes, Benzodiazepines and respiratory support⁴. The latest studies have revealed other mechanisms rather than Acetylcholinesterase inhibition like acute inflammation in Organophosphate poisoning syndromes emergence⁵. The relationship between being in contact with Organophosphate poisons and emergence of asthma symptoms and the increasing of airways stimulation have been revealed in new epidemiologic and clinical studies⁶.

Since there have seen no studies about the effects of dexamethasone on the reduction of mortality caused by Organophosphate poisoning and its pathologic effects on lungs, we decided to study this matter.

**METHODS**

This is an experimental study and it has been done on rats. 40 adult male rats with the approximate weight of 200-250 grams were divided into two groups of 20. The rats of each group were in the same state of living circumstances, temperature, water, consumed food and lightening and darkness cycles. Both groups were injected 25 mg/kg of diluted Dichlorvos poison in 0.09% saline subcutaneously. The cause of using this amount of the poison was for making sure of the death of all the rats of control group. In the same researches, using this dose caused death in 100% of control group in 12 minutes. Rats of control group received 0.5 ml of normal saline intraperitonealy one minute after being injected with the poison. Rats of treatment group received 100 mg/kg dexamethasone intraperitonealy one minute after receiving poison. Then both groups were analyzed for mortality and the time period of apnea. If a rat stayed alive for 120 minutes it was considered as a survived one. Their lungs were sent to pathology unit for further investigation. The sent samples were kept in 10% formalin for 24 hours. After preparing a block and a 5 micron slice of the samples, they were colored using H&E method. The pathologist reported at least 10 fields regarding the severity of inflammation and existence of parameters like Tissue necrosis.

**RESULTS**

10 rats of the treatment group survived (50%), while all the control group rats died, which shows a significant difference between the two groups (p value=0.033).

The average time of mortality in treatment group was 20/20±1/48 and in control group was 15/00±2/74, which is less than treatment group (p value = 0.002) (table 1).

<table>
<thead>
<tr>
<th>P Value</th>
<th>Standard deviation</th>
<th>Average</th>
<th>Number</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.48324</td>
<td>20.2000</td>
<td>10</td>
<td>Treatment</td>
</tr>
<tr>
<td>2.75874</td>
<td></td>
<td>15.0000</td>
<td>20</td>
<td>Control</td>
</tr>
</tbody>
</table>

**Table 2.** Frequency of first degree perivascular congestion in the analyzed samples

<table>
<thead>
<tr>
<th>P Value</th>
<th>Group</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0.007</td>
<td>control</td>
<td>0.00%</td>
<td>5.00%</td>
<td>Slight</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.00%</td>
<td>35.00%</td>
<td>mediocre</td>
</tr>
<tr>
<td></td>
<td></td>
<td>45.00%</td>
<td>10.00%</td>
<td>Severe</td>
</tr>
<tr>
<td></td>
<td>treatment</td>
<td></td>
<td></td>
<td>Vascular</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>congestion</td>
</tr>
</tbody>
</table>
In pathologic samples of dead rats these matters were observed:
The results showed that perivascular inflammation (p value=0.164), inflammation of the peribronchi (p value=0.500), neutrophilic exudation (p value=0.400), and alveolar wall thickening (p value=0.087) and hemosiderin existence (p value=0.806) don’t indicate a significant difference between the two groups. But first degree vascular congestion was significantly more in control group (p value=0.007) (table 2 and Diagram 1).
Second degree hemorrhage was also significantly higher in control group (p value=0.046) (Table 3).

<table>
<thead>
<tr>
<th>P Value</th>
<th>Group</th>
<th>Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05</td>
<td>5.00%</td>
<td>15.00% none Second</td>
</tr>
<tr>
<td></td>
<td>20.00%</td>
<td>30.00% slight degree</td>
</tr>
<tr>
<td></td>
<td>15.00%</td>
<td>5.00% mediocre hemorrhage</td>
</tr>
<tr>
<td></td>
<td>10.00%</td>
<td>0.00% severe</td>
</tr>
</tbody>
</table>

**Discussion**

in this experimental study there were 20 rats in each group. Rats of control group were injected with normal saline in addition to poison and rats of treatment group were injected with dexamethasone besides poison.

Dexamethasone is a strong Anti-inflammatory drug which prevents the hyper-excitability of airways in case of being in contact with Stimulating antigens. Prescribing dexamethasone can prevent the dysfunction of m2 muscarinic receptors (which is one of the mechanisms of allergic reaction increase in airways).

In a study done by DU et al, it was revealed that prescribing sodium aescinate (which has anti-inflammatory and Anti-oxidative effects) can prevent the pulmonary damages of organophosphate poisoning. In another study done by Proskocilek et al, it was revealed that organophosphate poisoning can result in the release of TNF-α from Pulmonary macrophages, the increase of allergic reactions in airways and the dysfunction of m2 muscarinic which can be prevented by prescribing Etanercept (a TNF-α Inhibitor).

This study revealed that the death rate is significantly less in control group and the time period to mortality is significantly more in treatment group. The pathologic results also revealed that perivascular inflammation, inflammation of the peribronchi, neutrophil exudation, alveolar wall thickening and hemosiderin existence don’t have a significant difference between two groups, but first degree vascular congestion and second degree hemorrhage was significantly more in control group. In a study done for this matter it was revealed that prescribing dexamethasone before being in contact with Parathion, which is an organophosphate poison, can increase Hepatic clearance from this poison by Induction of CytochromeP3A23 enzyme.

Dinis-Oliveira et al revealed in a related study that prescribing a high dose of dexamethasone for the rats that were in contact with parquat poison (which cause death by Respiratory failure) can reduce the mortality and improve the pathologic effects in treated rats. So it’s consistent with our study.

**Conclusion**

As a general matter it seems that dexamethasone can somehow reduce the destructive effects of organophosphate poisons in alveoli and also reduce the mortality significantly. Because of the limitation of the
number of the samples, more studies are needed to approve the results of this study.

REFERENCES


