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# Study of Histopathology of Rat Liver under the Effects of Dexmedetomidine during Experimental Sepsis

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## ABSTRACT

**Introduction:** The Food and Drug Administration Authority has approved a new antidepressant dexmedetomidine for use in critical care units. Dexmedetomidine is an imidazole compound with a high affinity for alpha-2 adrenoceptors, known for its anti-anxiety effect and minimal respiratory difficulty. Patients admitted to critical care units need prolonged sedation and require agents like dexmedetomidine. The leading cause of death in hospitals is sepsis which is a disorder resulting from the response of the host to infectious substances.

**Aims and Objectives:** The aim of the study is to identify the histopathological changes in rat liver on administering dexmedetomidine during septicemia.

**Place and Duration of study:** The study was conducted in the animal house of the Postgraduate Medical Institute, Lahore over 4 weeks.

**Material and Methods:** Ethical approval was obtained from the Ethical Committee at Postgraduate Medical Institute, Lahore. Female rats weighing 200-250 grams were taken for 4 weeks. One week before the experiment, animals were adapted in the lab maintained at 22 ± 2°C, with a continuous 12-hour light/dark cycle.. Data was entered and analyzed using SPSS version 25. P value of < 0.05 was considered statistically significant.

**Results:** The control group did not show any significant changes. Three mortalities were observed in the toxic groups Total scoring of pathological alterations in the liver was done. The hepatic tissue scoring of the control group was 0.4±0.52. In the septic group, it was 1.5±0.80 & in the dexmedetomidine groups it was 4.5±0.9. The differences in variations of tissues were statistically significant.

**Conclusion:** The study concludes that dexmedetomidine induces beneficial changes in the histopathology of rat liver during sepsis.


**Key Words:** Dexmedetomidine, Antidepressant, sepsis

## INTRODUCTION

Dexmedetomidine is an antidepressant used in critical care units.[1] Other qualities include antianxiety effect and minimal respiratory difficulties. Recent studies have shown it to be helpful in sedating pediatric patients in hospitals.[2,3] Dexmedetomidine has proven to be helpful in decreasing duration of dizziness in different patients.[4] Different experimental studies revealed that dexmedetomidine has defensive role in prevention of oxidative toxicity.[5,6] Other studies have shown that dexmedetomidine is protective in reperfusion injury dexmedetomidine is protective in reperfusion injury due to ischemia. Experimental studies also revealed the beneficial effects of dexmedetomidine on pulmonary functions.[7]

In different studies dexmedetomidine has shown to inhibit organ damage i.e. liver & kidney and inflammatory response. Beneficial effects of dexmedetomidine include better sedation & hemodynamic stabilization.[6,8] Leading cause of death in hospitals is sepsis which is a disorder resulting from response of host to infectious substances.[9] Patients admitted in critical care units need prolong sedation require agents like dexmedetomidine. The purpose of this study is to explain the histopathological changes of dexmedetomidine liver during septicemia in rats.

## MATERIALS AND METHODS

The study was conducted in the animal house of Postgraduate Medical Institute, Lahore. Our study got ethical approval by the Ethical Committee of Postgraduate Medical Institute, Lahore under IRB

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No – UHS /Education/135-12/85. Female rats weighing 200-250 grams were used for 4 weeks. One week before the experiment, animals were adapted in the lab maintained at a temperature of 22 ± 2°C, with a continuous 12-hour light/dark cycle. Rats were kept in iron cages and fed with regular diet.

**Grouping of animals:**

Animals were randomly assigned to three groups:

1. Toxic group (n=8): Toxemia was introduced by injection of E.coli administered IV at 12mg/kg over 2 min.
2. Toxic group with dexmedetomidine (n=8). Toxicity was induced and dexmedetomidine was given IV at 15mg/ kg over 4 min.
3. Control group (n=8): In this group animals were treated with 0.8% saline.

**Histological Examination:**

After six hours of toxin infusion, with 250 mg /kg of pentathlon sodium, all rats were sacrificed and a median laparotomy was conducted to separate the livers. Livers were resected and immersed in 12% formaldehyde for 20 hours and fixed into paraffin after 14 hours of processing with alcohol treatment. Six micrometer thick sections were separated from paraffin blocks and staining was done with eosin and hematoxylin. The pathologist examined each slide under a light microscope. Congestion of central veins, enlargement of hepatic sinusoids, and swelling of portal tracts were observed and grading was done from 1- 4.[6]

**Grade 1**: showing no change,
**Grade2**: showing minimal changes,
**Grade3:** presenting medium changes
**Grade4:** with extreme effects

Collection of all grades was considered as a total score ranging from 1-4.

**Statistical Analysis:**

The results were expressed as mean ± SD. The Kruskulwallis test was used to compare differences among groups. Then Student–Newman-Keuls post-hoc test was used when a significant difference was found. P value of <0.05 was considered statistically significant.

## RESULTS

Three rats from toxic group showed severe engorgement of central veins while other rats showed moderate congestion. Five rats showed mild engorgement of central vein in dexmedetomidine group. Statistically significant difference was appreciated in two groups with p value <0.001. Eight rats of dexmedetomidine group presented with mild venous engorgement.

Severe inflammation was seen in portal system of livers of septic group while only two moderate portal system swellings were observed in dexmedetomidine group. Statistically significant difference was found between two groups p-value <0.002.

**Fig-1: No Change in hepatic sinusoids & central vein of control group**

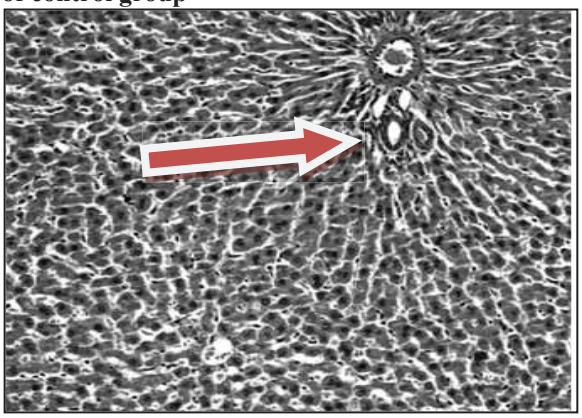


**Fig-2: Mild Change showing edema & some congestion of hepatic sinusoids of dexamedetomidine treated toxic group**

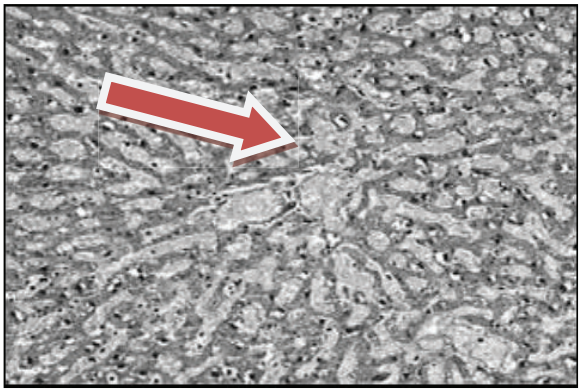


**Fig-3: Moderate change resulting in congestion of central vein and engorgement of sinusoids in E. coli treated group.**

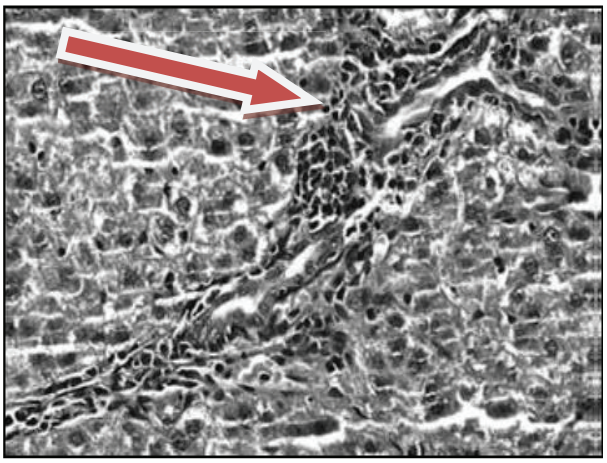
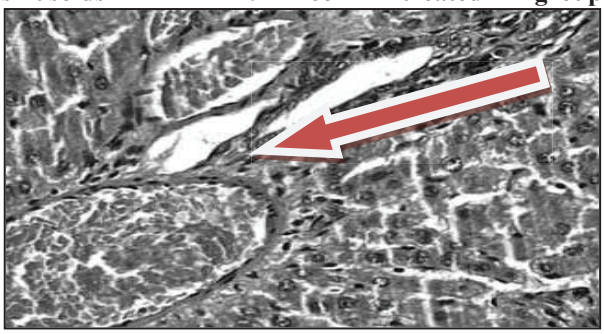


**Fig-4: Severe Changes showing marked congestion of central vein & extensive enlargement of hepatic sinusoids in E. coli treated group.**



Control group did not show any change. Three mortalities were observed in toxic groups Total scoring of pathological alterations in liver was done. Tissue scoring of control group was 0.4± 52. In septic group it was 1.5±0.80 & in dexmedetomidine group it was 4.0± 0.9. The mean of total scoring of variations of tissues showed a statistically significant difference in groups (p-value <0.002). Table shows the results of tissue variables.

**Table 1: showing comparison of groups with reference to P-values**

| Tissue effects | Control (n=8) | Dexmedetomidine (n=8) | Sepsis (n=8) | P-value |
|---|---|---|---|---|
| **Congestion of central vein** | 0.25 ± 0.40 | 0.6 ± 0.53 | 3.4 ± 0.52 | <0.002 |
| **Sinusoidal obstruction** | 0.020 ± 40 | 0.2 ± 0.42 | 1.2 ± 0.42 | <0.001 |
| **Swelling of portal tracts** | 0.01 ± 0.02 | 0.8 ± 0.5 | 1.8 ± 0.53 | <0.002 |
| **Total** | 0.03 ± 0.52 | 1.6 ± 0.72 | 4.5 ± 0.02 | <0.001 |

## DISCUSSION

The study aimed to evaluate the beneficial effects of dexmedetomidine on liver tissue of septic rats. It was assumed that dexmedetomidine reduces liver destruction related to toxicity and shock. Toxemia is a leading cause of death in critical care units and treated on urgent basis. It was observed that dexmedetomidine lowers congestion of central veins. Similar changes were observed in another study where dexmedetomidine reduced liver toxicity caused by lipopolysaccharides.[10]

Another study revealed that tissue ischemia of liver tissue caused by hypoxia is less with dexmedetomidine[11]. Similar findings were also observed in another study in which histopathological effects of anabolic steroid sustanon were observed on liver of male rats.[7] Sections of liver showed cellular inflammation, degeneration of hepatocytes and apoptosis in period of 3-4 weeks. It was also observed that dexmedetomidine treated group had less inflammation & congestion of hepatic sinusoids. Studies demonstrated that dexmedetomidine exhibit anti-inflammatory & antioxidant properties & has hepatoprotective effect in different cases of hepatic jaundice.[12-14]

Another study revealed that dysfunction of liver is the most common form of injury seen in septic patients where it leads to liver failure a grave complication. So, it is important to understand the pathophysiological changes that contribute to liver dysfunction associated with sepsis.[10]

Another study revealed that perioperative administration of dexmedetomidine can exert a protective effect on liver injury after hepatectomy.[12] Dexmedetomidine is highly effective in treating liver toxicity caused by infection. This study revealed that dexmedetomidine is effective for treating liver toxicity caused by infection.

## CONCLUSION

Our study has shown the protective effect of dexmedetomidine in liver destruction due to toxicity.

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**Authorship:**

**SM:** Proposal of article
**FI :** Helped in methodology
**MS:** Evaluation of histological results
**NM**: Statistic analysis
**HG**: Discussion details
**RJ:** References