Original article

Role of Intravenous Paracetamol Infusion in Surgical cases of Systemic Inflammatory Response Syndrome

***Kunal H. Sayani[1], Anant A. Dawange[2], Nidhi D. Rathi[3], Dattaguru R. Kulkarni[4]**

[1]Assistant Professor, Department of Surgery, Government Medical College, Akola, Maharashtra , 444001, India
[2]Associate Professor, Department of Surgery, Government Medical College, Akola, Maharashtra , 444001, India
[3] Tutor, Department of Physiology, Government Medical College, Akola, Maharashtra-444001, India
[4]Professor, Department of Surgery, Grant Government Medical College, Mumbai, Maharashtra , 400001, India
Corresponding author: Kunal H. Sayani ,Assistant Professor, Department of Surgery, Government Medical College, Akola, Maharashtra-444001, India

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Abstract:

Systemic Inflammatory Response Syndrome is a serious condition related to systemic inflammation, if untreated in time can lead to organ dysfunction & death. The purpose of this study was to evaluate the effects of antipyretic therapy on patients presenting with features of SIRS.In this study out of 100 selected cases, 50 were randomly assigned to the study group and 50 to the control group. The study group received intravenous paracetamol infusion while the control group was observed. The study found that intravenous paracetamol infusion reduced pulse rate, respiratory rate and temperature significantly in study group as compared to control group. Thus intravenous paracetamol infusion has a role in controlling symptoms and signs of SIRS in its early phase.

Keywords: Systemic Inflammatory Response Syndrome

Introduction

Systemic Inflammatory Response Syndrome (SIRS) is a serious condition related to systemic inflammation, organ dysfunction and organ failure. It is a subset of "cytokine storm", in which there is abnormal regulation of various cytokines. SIRS is also closely related to Sepsis, in which patient satisfy the criteria of SIRS and have a suspected or proven infection.

Criteria for SIRS were established in 1992 as part of the American College of Chest Physicians/Society of Critical Care Medicine:

- Body temperature less than 36°C(96.8°F) or greater than 38°C(100.4°F)
- Tachypnea (high respiratory rate), with greater than 20 breaths per minute
- Heart rate greater than 90 beats per minute
- An arterial partial pressure of carbon dioxide less than 4.3 kPa (32 mmHg)
- White blood cell count less than 4000 cells/mm³ (4 x 10^9 cells/L) or greater than 12,000 cells/mm³ (12 x 10^9 cells/L); or the presence of greater than 10% immature neutrophils (band forms)

SIRS can be diagnosed when two or more of these criteria are present. These changes should represent an acute change from baseline and be unexplained by other causes.

The causes of SIRS are broadly classified as infectious or noninfectious. When SIRS is due to an infection, it is considered 'sepsis'. Noninfectious causes of SIRS include trauma, burns,pancreatitis,appendicitis,ischemia, hemorrhage, etc.

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The purpose of this study is to evaluate the effects of antipyretic therapy on patients presenting with features of SIRS in emergency surgical ward of a tertiary care hospital. We hypothesized that optimal application of antipyretic therapy in the form of intravenous paracetamol infusion improves clinical outcomes in patients with SIRS.

Aims & Objectives

1. To study the clinical presentation and pathophysiology of Systemic Inflammatory Response Syndrome.
2. To study the actions, indications and effects of intravenous paracetamol infusion.
3. To study the role of intravenous paracetamol infusion, as an additivetreatment inselective emergency surgical cases of S.I.R.S.

Materials& methods

This study was conducted in a period of two years in the department of surgery, Government Medical College on patients presenting with features of S.I.R.S. (SYSTEMIC INFLAMMATORY RESPONSE SYNDROME) in an emergency surgical ward.

The study was carried out after the prior permission from the institution's local ethical committee. All the patients agreed to take part in the study.In this study,100 patients were randomly selected out of all emergency admissions in a general surgical ward, who presented with features of Systemic Inflammatory Response Syndrome viz.,Acute appendicitis,Acute pancreatitis,Acute cholecystitis, Peritonitis,Trauma & Burns.. All patients were in the age group of 18-60 years.

Both groups were treated as per standard treatment regimen using intravenous fluid resuscitation, antibiotics, analgesics and antacids, with due consideration of clinical condition of respective patient.

Intervention in the form of intravenous paracetamol infusion (10mg/kg – 1g, 8 hourly) was given to 50/100 randomly selected patients in addition to their standard treatment regimen and their disease progress and vital parameters were monitored periodically over 72 hours. WBC counts of patients were recorded using venous blood samples at 6h, 12h, 24h, 48h and 72h intervals.

The other group of patients wasalso treated as per standard protocol but intravenous paracetamol infusion was not administered unlessthey developed fever. The rise in temperature was recorded and antipyresis was done immediately with administration of paracetamol. This group was also monitored in similar way, over the same time interval. The results were then tabulated and data analysis was done.

Statistical Analysis: All the collected data was entered in Microsoft Excel sheet. It was then analysed using SPSS ver.17 software for statistical analysis. Quantitative data was presented as mean and standard deviation and compared using student's t-test. Qualitative data was presented as frequency and percentage and analysed using chi-square test. P-value of <0.05 was considered as significant and <0.01, as highly significant.

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Observations & Results

In this study following observations were made.

Gender	Group		Total
	Case	Control	
Female	23	20	43
Male	27	30	57
Total	50	50	100
p- value - 0.54			

The above table shows the equal distribution of patients in both, study group and control group.

Diagnosis	Case	Control	Total
Acute Appendicitis	8	8	16
Acute Cholecystitis	10	10	20
Acute Pancreatitis	12	12	24
Polytrauma	12	12	24
Burns	8	8	16
Total	50	50	100
p- value – 1			

The above table shows that out of total 100 patients, 16 patients were diagnosed with acute appendicitis, 20 with acute cholecystitis, 24 with acute pancreatitis, 24 with polytrauma and 16 patients with burns. Cases and controls were divided equally in 1:1 ratio, as per their diagnosis.

Group	N	Mean Age (years)	SD	SEM	p- value
Case	50	35.02	10.338	1.462	**0.86**
Control	50	34.64	10.751	1.52	

The above table shows that the mean age of cases was found to be 35.02 years and that of controls, 34.64 years. p-value of 0.86 indicates both groups are statistically comparable as regards to their ages.

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Pulse Rate	Group	N	Mean	SD	SEM	p- value
On Admission	**Case**	50	126.8	8.4	1.2	**0.32**
	Control	50	125.1	8.7	1.2	
6 hours	**Case**	50	117.1	8.2	1.2	**0.60**
	Control	50	118.0	9.3	1.3	
12 hours	**Case**	50	115.6	7.6	1.1	**0.17**
	Control	50	118.0	9.4	1.3	
24 hours	**Case**	50	112.9	7.2	1.0	**0.02**
	Control	50	116.7	9.1	1.3	
48 hours	**Case**	50	107.7	6.6	0.9	**< 0.01**
	Control	50	114.2	9.2	1.3	
72 hours	**Case**	50	102.0	6.9	1.0	**< 0.01**
	Control	50	110.1	9.4	1.3	

The above table showsmean pulse rate on admissionof cases was found to be **126** and that of control group was **125**. p-value of 0.32 indicated the two groups were comparable at the time of admission. After the intervention, the comparison of parameter - pulse rate was analysed and respective p-values were calculated, as mentioned above. The difference was found to be significant at 24h (0.02) and highly significant (<0.01) at 48h and 72h recording, indicating that our intervention reduced the pulse rate significantly in the study group.

Respiratory Rate	Group	N	Mean	SD	SEM	p- value
On Admission	**Case**	50	27.0	4.1	0.6	**0.58**
	Control	50	26.5	4.1	0.6	
6 hours	**Case**	50	24.6	3.6	0.5	**0.72**
	Control	50	24.9	4.2	0.6	
12 hours	**Case**	50	23.8	3.2	0.4	**0.30**
	Control	50	24.5	4.1	0.6	
24 hours	**Case**	50	22.5	2.5	0.4	**0.03**
	Control	50	23.8	3.7	0.5	
48 hours	**Case**	50	20.7	1.9	0.3	**< 0.01**
	Control	50	23.1	3.9	0.6	
72 hours	**Case**	50	19.7	1.6	0.2	**< 0.01**
	Control	50	21.8	3.3	0.5	

The above table shows mean respiratory rate on admission of cases was found to be **27** and that of control group was **26.5**. p-value of 0.58 indicated the two groups were comparable at the time of admission. After the intervention, the comparison of parameter – respiratory rate was analysed and respective p-values were calculated, as mentioned in the above table. The difference was found to be significant at 24h (0.03) and highly

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significant (<0.01) at 48h and 72h recording, indicating that our intervention reduced the respiratory rate significantly in the study group.

PaCO2	Group	N	Mean	SD	SEM	p- value
On Admission	**Case**	50	31.0	3.8	0.5	**0.79**
	Control	50	31.2	3.8	0.5	
72 hours	**Case**	50	37.2	3.1	0.4	**0.58**
	Control	50	36.8	3.7	0.5	

The above table shows mean $PaCO_2$ on admission of cases was found to be **31** and that of control group was **31.2**. p-value of 0.79 indicated the two groups were comparable at the time of admission. After the intervention, the comparison of parameter – $PaCO_2$ was analysed at 72h. The difference was found to be insignificant (0.58).

Temperature	Group	N	Mean	SD	SEM	p- value
On Admission	**Case**	50	38.3	0.8	0.1	**0.73**
	Control	50	38.4	0.7	0.1	
6 hours	**Case**	50	37.9	0.6	0.1	**0.65**
	Control	50	37.9	0.6	0.1	
12 hours	**Case**	50	37.8	0.6	0.1	**0.08**
	Control	50	38.0	0.6	0.1	
24 hours	**Case**	50	37.6	0.6	0.1	**< 0.01**
	Control	50	37.9	0.6	0.1	
48 hours	**Case**	50	37.3	0.5	0.1	**< 0.01**
	Control	50	37.8	0.6	0.1	
72 hours	**Case**	50	37.1	0.5	0.1	**< 0.01**
	Control	50	37.7	0.5	0.1	

The above table showsmean temperature of cases at the time of admission was found to be **38.3^{o}C** and that of control group was **38.4^{o}C**. p-value of 0.73 indicated the two groups did not differ significantly at the time of admission, as regards to their baseline temperatures. After the intervention, the comparison of parameter – temperature was analysed and respective p-values were calculated as mentioned in the above table. The difference was found to be highly significant from 24h onwards (<0.01)

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WBC Count	Group	N	Mean	SD	SEM	p- value
On Admission	**Case**	50	13868.8	4757.3	672.8	**0.88**
	Control	50	13732.4	4561.3	645.1	
6 hours	**Case**	42	14125.8	4724.4	729.0	**0.69**
	Control	42	13709.9	4777.2	737.1	
12 hours	**Case**	42	13942.1	4664.5	719.8	**0.76**
	Control	42	13630.8	4724.8	729.1	
24 hours	**Case**	50	13471.6	4447.5	629.0	**0.90**
	Control	50	13354.0	4472.4	632.5	
48 hours	**Case**	50	13140.4	4254.8	601.7	**0.87**
	Control	50	12998.6	4284.6	605.9	
72 hours	**Case**	50	12650.4	3924.2	555.0	**0.98**
	Control	50	12627.7	4099.1	579.7	

The above table shows mean WBC counts of the study group at the time of admission was **13868** and that of control group was **13732**. p-value of 0.88 indicated that the two groups were statistically comparable at the time of admission with respect to their WBC counts. After the intervention, WBC counts were recorded and analysed and respective p-values were calculated as tabulated above. However, even after 72h, there was no significant difference between the two groups, indicating that our intervention had no effect on WBC counts.

Discussion

Both the groups, i.e. study group and control group had 50 patients each. Patients in both the groups were comparable with respect to their age and diagnoses.

The proposed mechanism for decreasing pulse rate is via blocking release of stress hormones like Norepinephrine,Vasopressin and Renin-Angiotensin-Aldosterone-System also observed by Michael Ryan *et al[1]*. It also blocks the production of pro-inflammatory cytokines like prostaglandins, leukotrienes and interleukins by inhibiting COX enzyme. A secondary mechanism may also be involved : controlling fever decreases

The Mean Respiratory Rate of our study group differed significantly (p = 0.03) from the control group starting from 24h onwards. The mean daily respiratory rate was lower in our study group as compared to control group (at 72 hours : it was 19 cycles per minute and 21 cycles per minute,

The respiratory rate is also secondarily resolved by controlling body temperature, which thereby decreases metabolic activity and CO_2 productionwhich was also observed by O'Dempsey TJ *et al [2]*

$PaCO_2$ showed similar normalisation in both the groups. The Mean $PaCO_2$ at 72 hours was 37.2 mmHg in the study group and 36.8 mmHg in the control group. p-value of 0.58 suggests that there is no significant difference between the two groups. Thus intravenous paracetamol infusion seems to have no effect on $PaCO_2$ when administered to patients of SIRS.

The Mean Temperature of the two groups showed highly significant difference (p = <0.01) from 24h onwards.The daily Mean Temperature was lower in the study group as compared to the control group (at 72 hours : 37.1^{o}C and 37.7^{o}C respectively). This indicates that our intervention reduced the temperature of the patients in the study group

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significantly as compared to those in the control group. So our study shows a definitive role of intravenous paracetamol infusion in lowering temperature of patients with SIRS. The same findings were observed by Honarmand H *et al[3]*, Gozolli V., Treggiari MM,*et al[4]* &Niven DJ *et al[5].*

The proposed mechanism for antipyretic effect of intravenous paracetamol is via blockage of TNF-α and IL-1 production, more pronounced in the CNS. This is achieved by inhibiting COX enzyme and preventing activation of NF-kβ . This is in accordance with the various studies done by Michael Ryan *et al[1]*, Malhotra V *et al[6].*

The WBC Count showed similar reduction in both the groups. The mean WBC counts of the two groups at the end of 72 hours were12650 in study group and 12627 in control group. p-value of 0.98 indicates that intravenous paracetamol infusion seems to have no significant effect on reducing WBC counts of patients with SIRS.The insignificant difference between the two groups can be explained by the weak anti-inflammatory action of paracetamol.

The same findings were observed by Burke A et al[7],Schulman CIet al[8]&Gozzoli V., Schottker P., et al [9].

Conclusion

- We concluded that intravenous paracetamol infusion reduced pulse rate, respiratory rate and temperature significantly in study group as compared to control group.
- There was no effect on $PaCO_2$ and WBC counts after administration of intravenous paracetamol due to its weak anti-inflammatory action.
- Thus intravenous paracetamol infusion has a role in controlling symptoms and signs of SIRS in its early phase. So it could be used as an additive treatment for patients presenting with SIRS.

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