

Study of Pinak in Covid 19 Patients As Adjuvant Treatment

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INTRODUCTION:

Second largest populous country India is suffering a worst epidemic of Covid 19 infection which India is seeing for the first time. During this pandemic many countries suffered worst epidemic with lakhs of people suffering from Covid 19 and thousands of people dying due to it. Wave of fear spread across globe as there was no medical cure of the disease. 10 to 15% people landing in ICUs. There was high death rate initially as knowledge of Covid 19 disease was meager. Researchers all over world started to try and find a medical treatment for Covid 19. During this study period, high end injections like Remdesivir, Tocilizumab were not available. Initially those injections were not within reach of the common people. Plasma therapy was also available at limited places as permission of ICMR is required for it.

In spite of a big fear initially, India took best decisions to control epidemic and restrict mortality. Ayush department of India took a best decision to try any Ayush drug to tackle epidemic. SKNMC & GH decided to conduct trials using a Pinak tablet as an Add on drug. Tablet Pinak is originally researched as antivenin drug to be used against snake bites, scorpion stings and honey bee bites. Pinak is an Ayurvedic herbal tablet licensed by FDA Maharashtra. Indication of the Pinak is 'As directed by Physician'. Possible mode of action of Pinak in snake bites etc. is by neutralizing the protein venom as seen from various snake bite studies showing neuro paralytic signs caused by Cobra disappear within 12 minutes of administration of Pinak sublingually suggesting rapid degradation / neutralization of venom from neurosynapses.

In Ayurveda, viral infection is treated as VISH⁴ / poison. Covid 19 attaches to host cells by 'S' proteins¹. If this 'S' protein is made ineffective,

virus will be degraded and virus will not be able to attach to host cells and disease will not progress further. Moreover, pathophysiology of Corona and viper snake bite^{2,3} appears similar, clinically as well as laboratory wise. Ingredients of Pinak are active^{5,6,7} against many viruses. Hence, we designed this clinical study with Pinak tablet as an adjuvant to protocol treatment.

Ingredients of Pinak are: Jusminum Sambac, Mangifera Indica, Eugenia Jambolana and Erythrina Indica.

Pinak is an oral/sublingual, Safe (LD 50 > 2000 mg/kg), herbal tablet.

METHODS:

This is Simple Randomized control parallel arm study design.

Randomization was stratified according to the category of the patient shown below in the table. Mild patients were of category A, B, & C. Moderate and severe patients were from category D & E. Critical (very severe disease with respiratory or multiorgan failure) patients are not included in the study. Patients with RT PCR or RAT positive were included in the study.

Present study was conducted in Smt. Kashibai Navale Medical College & General Hospital Medicine Department in Covid hospital from 22-05-2020 to 17-09-2020.

Control group was given only Protocol drugs recommended by Government as per the clinical category of the patient. Covid-19 management protocol for Covid-19 adult patients was issued by DMER and DHS, Mumbai on 30 March 2020. It includes A, B, C, D and E categories of Covid-19 patients. These categories are based on clinical manifestations, presence of Pneumonia and presence of co morbidities.

Table Showing categories of Covid 19 patients:

Category	Patients included
A	Asymptomatic patients (covid positive) who are without any co morbidity or with co morbidity
B	Symptomatic patients without any co morbidity
C	Symptomatic patients with any one or more co morbidity
D	Symptomatic patients with pneumonia without ARDS
E	Symptomatic patients with severe pneumonia with respiratory failure or multiorgan failure

In Pinak study group for mild cases group, Pinak was given orally in 1 tablet tid doses and for moderately severe cases group, 2 tablets stat and then 1 tablet Qid was given orally.

Primary outcome: To study whether Adjuvant administration of tablet PINAK enhances Recovery from Covid – 19 infection.

Secondary outcomes:

1. To study whether adjuvant administration of tablet PINAK reduces Morbidity and Mortality in Covid – 19 patients.
2. To study whether adjuvant administration of tablet PINAK reduces progression of the disease to the need of O2 support or ventilator support.
3. To study whether adjuvant administration of tablet PINAK reduces evolution of secondary events like ACS, CVA, and Pulmonary embolism.

All patients were strictly observed for signs & symptoms to assess status of patient and

recorded the observations on case paper file. Appropriately required investigations were done for proper assessment. Any Relief or Increase in signs and symptoms noted on case papers. Progression or regression of disease compared with corresponding laboratory markers. Any effect of co morbidity was noted. Duration of O2 therapy/ ventilator time noted accurately.

This is a pilot study. Sample size is minimum 30 patients.

Randomization: Patients are stratified in two groups as Mild and Moderate & Severe Then Simple randomization method is used. Eligible patients were randomly assigned (1:1)(daily n is even)/(2:1)(daily n is odd) to either the Pinak group or the Control group.

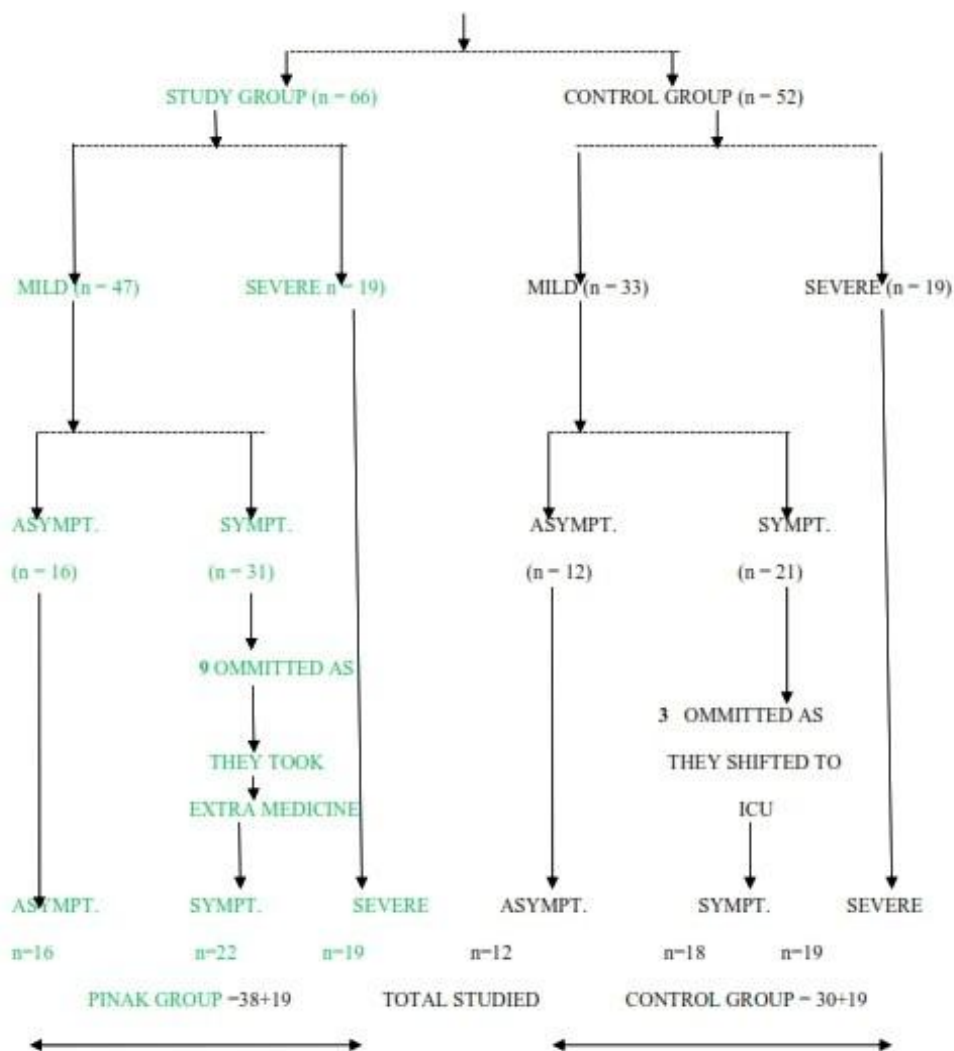
In Covid hospital, incharge staff prepared daily list of admissions who were Covid 19 positive. This list was taken by an independent controller daily. If number of admissions is even, random two equal blocks were done. If number was odd, then two random blocks in 2:1 ratio were done. Controller informed the doctor on duty which patient is assigned in which group. In Pinak study group, informed consent of each patient was taken before administration of drugs.

STATISTICAL METHODS:

Data was collected, compiled and tabulated with help of Microsoft Excel 2007. Continuous variables such as age, BP, SpO2 were expressed as mean, Standard deviation (SD) and categorical variables such as symptoms, hospital stay were expressed as proportions.

Association between attributes were tested by two sample t test, Chi-square test and fisher's exact test with help of Epi-Info and Open-Epi statistical software.

RESULTS:Participants flow diagram: TOTALPTS (n = 118)



Recruitment:

Recruitment of patients of Mild category was done from 22-05-2020 to 24-07-2020. We enrolled Moderately severe patients from 22-05-2020 to 07-09-2020 as number of patients admitted daily is less as compared to the Mild group.

We tried to enroll maximum patients for better results. When we enrolled 57 patients (38 in mild & 19 in moderate, severe groups) for Pinak study group and 49 patients (30 in mild & 19 in moderate, severe group) for Control group; we stopped enrollment of patients.

ENROLLED PATIENTS FOR STUDY

(Asymptomatic and Mild group)

Pinak study Group n = 47				Control Group n = 33			
Group	Details	Studied pts	Total studied	Group	Details	Studied Pts	Total Studied
Asymptomatic		16	16	Asymptomatic		12	12
Mild	Enrolled	31	22	Mild	Enrolled	21	18
	Omitted as took more ayurvedic drugs	9			Transferred To Covid ICU as they worsened	3	
	Studied	22			Studied	18	
Total studied			38	Total studied			30

(Moderate and Severe group)

1. PINAK study group = 19
2. Control group = 19

BASELINE DATA & ANALYSIS FOR MILD CATEGORY PATIENTS:

Table 1: Age and Sex Wise Distribution

AGE GROUP	Pinak(n=38)			Control(n=30)		
	Male(%)	Female(%)	Total(%)	Male(%)	Female(%)	Total(%)
15 - 30	5 (13.16)	5 (13.16)	10 (26.32)	6 (20)	6 (20)	12 (40)
30 - 45	9 (23.38)	7 (18.42)	16 (42.11)	4 (13.33)	5 (16.67)	9 (30)
45 - 60	2 (5.26)	9 (23.68)	11 (28.95)	2 (6.67)	4 (16.67)	6 (20)
>60	0	1 (2.63)	1 (2.63)	3 (10)	0	3 (10)
Total	16 (42.11)	22 (57.89)	38 (100)	15 (50)	15 (50)	30 (100)

Table 2: Distribution According to Presence of Symptoms

Symptoms	Pinak		Control	
	Frequency	%	Frequency	%
Yes	22	57.89%	18	60.00%
No	16	42.11%	12	40.00%
Total	38	100.00%	30	100.00%

Table 2.1: Distribution According to Type of Symptoms

Symptoms	Pinak(n=22)		Control(n=18)	
	Frequency	%	Frequency	%
Cough /sore throat	14	63.64	12	66.67
Running Nose	2	9.09	0	0.00
Fever	11	50.00	9	50.00
Breathlessness	7	31.82	3	16.67
Chills	1	4.55	0	0.00
Myalgia	6	27.27	8	44.44

Modified Table 2.2: Distribution According to Type of Symptoms

Symptoms	Pinak(n=22)		Control(n=18)		p Value*
	Frequency	%	Frequency	%	
URTI type	16	87.5	12	66.7	P>0.05
Fever/chills	12	68.75	9	50.0	P>0.05
Breathlessness	7	43.75	3	16.7	P>0.05
Myalgia	6	37.5	8	44.4	P>0.05

*Calculated by Fisher exact/Mid-P exact

No significant difference was observed in distribution of symptoms in both groups

Table 3: Distribution of Co-Morbidity

Co morbidity	Pinak(n=38)		Control(n=30)	
	Frequency	%	Frequency	%
DM	2	5.26	2	6.67
HTN	5	13.16	5	16.67
Other	3	7.89	4	13.33
Total*	10	26.32	11	36.67

Other: IHD, CKD, Asthma, Epilepsy

*P >0.05

In Pinak group 10(26.32%) patients have co morbidities while in control group 11(36.67%) patients have co morbidities.

No significant statistical difference is observed by chi square test. (p >0.05)

Table 4. Baseline Parameters in Both Groups

Sr. No.	Parameter	Pinak (SD), n=38	Control (SD), n=30	t	P
1	Mean Age	39.74(12.38)	37.77(15.66)	0.56	> 0.05
2	HB	12.7(2.01)	12.53(1.90)	0.37	> 0.05
3	TLC	5856.58(2097.75)	6065.33(1854.05)	-0.43	> 0.05
4	N/L ratio	1.66(0.84)	1.88(1.34)	-0.78	> 0.05
5	Platelet count	238368.42(66420)	222633.33(76436)	0.89	> 0.05
6	Bilirubin	0.57(0.39)	0.62(0.3)	-0.61	> 0.05
7	SGOT	38.03(24.39)	31.93(5.45)	1.49	> 0.05
8	SGPT	37.37(44.33)	25.67(10.8)	1.57	> 0.05
9	ALP	84.26(33.51)	77.73(18.53)	1.03	> 0.05
10	LDH	204.08(49.44)	202.7(49.37)	0.12	> 0.05
11	BSL	101.78(24.28)	113.23(45.5)	-1.24	> 0.05
12	Blood Urea	29.42(8.4)	26.47(10.9)	1.22	> 0.05
13	SPO2	98.03(0.99)	97.77(1.59)	0.99	> 0.05
14	Pulse Rate	83.16(7)	82.67(6.4)	0.30	> 0.05
15	RR	18.03(2.3)	18.27(1.3)	-0.55	> 0.05

No significant difference in Control group and Pinak treatment group.

Table 5: Effect of Drug Pinak on Symptomatic Relief (days required) in Mild Symptomatic Group

Parameter	Pinak(n=22)	Control(n=18)	t	P
Symptomatic relief	3.14(1.8)	6.39(3.6)	-5.29	< 0.01*

*Statistically significant

**Table 6: Showing No. of Patient's Symptom Free on Day From
DATE OF ADMISSION**

Day	Pinak group	Control group
2	4	1
3	4	1
4	6	2
5	3	3
6	2	2
7	2	2
8	0	3
9	1	3
10	0	1

Graph No. 1: Showing No. of Patient's Symptom Free on Day from Date of Admission

NO. OF PATIENTS

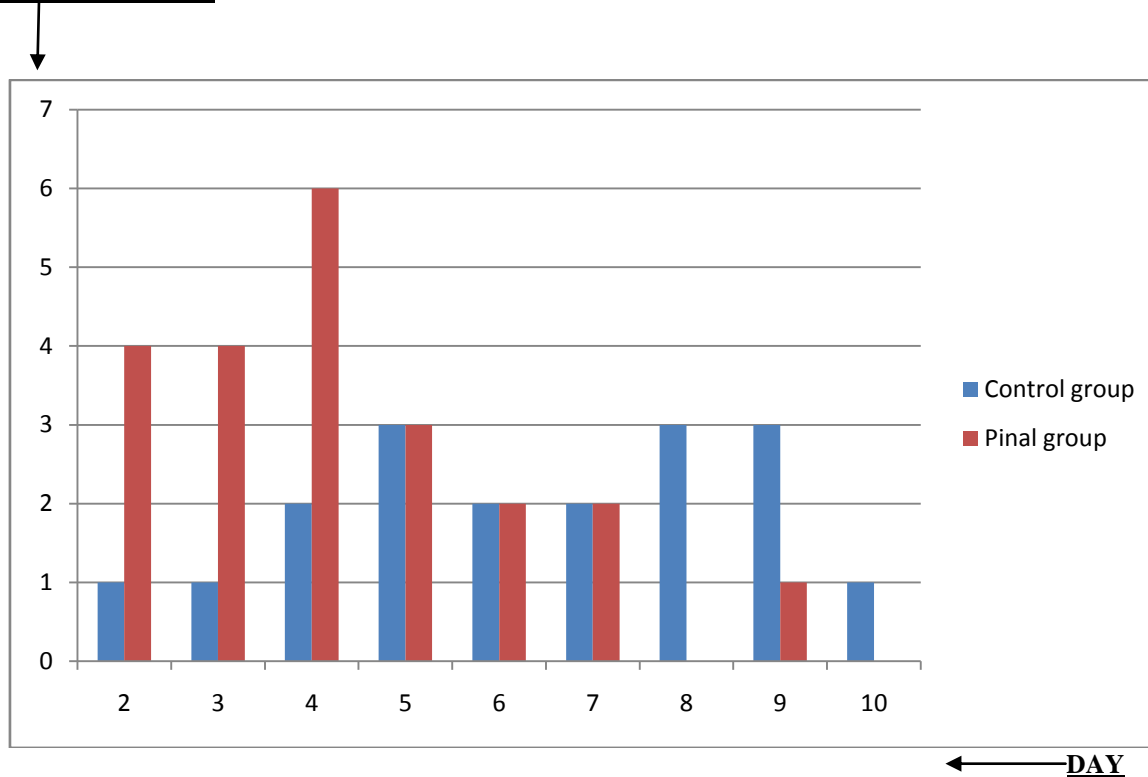


Table7:Showing Number of Patients Becoming Symptom Free on Respective Day from DAY OF PINAKSTARTED

Day Symptoms Relieved	Pinak Study Group	Control Group
2	10	1
3	6	1
4	2	2
5	3	3
6	0	2
7	1	2
8	0	3
9	0	3
10	0	1

Graph 2: Showing Number of Patients Becoming Symptom Free on Respective Day from DAY OF PINAK STARTED

NO. OF PATIENTS

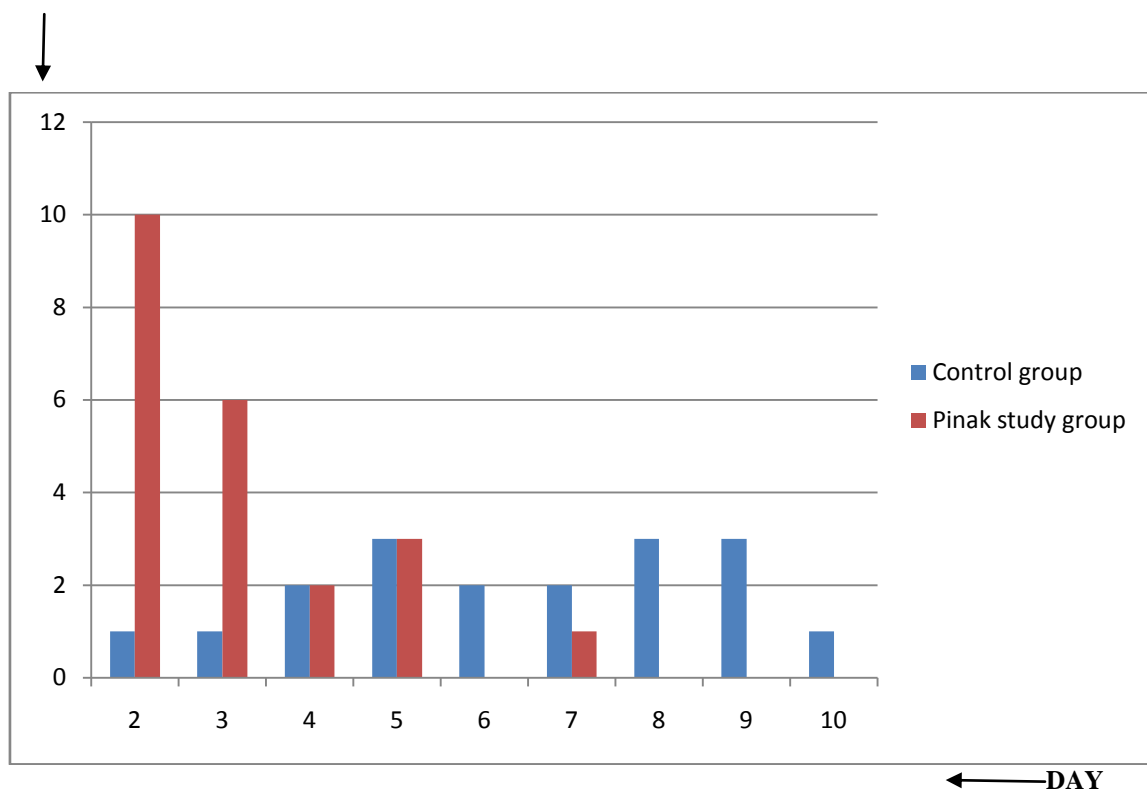


Table 8: Significantly Early Recovery in Patients Who Had Taken Pinak as Compared to Control Group (from Table no. 9)

Day of Symptomatic Recovery	Pinak (n = 22)		Control (n = 18)		p*
	Cumulative Frequency	%	Cumulative Frequency	%	
3rd day	16	72.73*	2	11.11	< 0.05
5th day	21	95.45*	7	38.89	< 0.05
7th day	22	100.00*	11	61.11	< 0.05

Fisher or Mid – P exact tests

Table 9: Table Showing Post Treatment Swab Testing after 5 Days in Mild Symptomatic Group

No of patients tested	Swab Negative	Swab positive
8	4 (50%)	4(50%)

Table 10: Showing Outcome of The Patients of Mild Category

	Pinak Study Group (n = 38)			Control Group (n = 30 + 3)		
	Discharged	Transferred to Covid ICU	Death	Discharged	Transferred to Covid ICU	Death
Number	38	0	0	30	3	0
Total	38	0	0	30	3	0

BASELINE DATA & ANALYSIS FOR MODERATE, SEVERE CATEGORY PATIENTS:

Table 11: Mean Age in Both Groups

Parameter	Pinak n=19(SD)	Control n=19(SD)	t	p
Age	54.42(12.38)	58.8(10.4)	0.12	> 0.05

Mean age in study group is 54.42 years with SD 12.38 while in control group is 58.8 years with SD 10.4 years. Difference is **not significant** and groups were comparable

Table 12: Gender Wise Distribution

Gender	Pinak(n=19)		Control(n=19)	
	Frequency	%	Frequency	%
Male	10	52.63	15	78.95
Female	9	47.37	4	21.05
Total	19	100.00	19	100.00

Table 13: Co Morbidities in Both Groups

Co morbidity		Pinak(n=19)		Control(n=19)	
		Frequency	%	Frequency	%
Yes	Single	7	36.84	8	42.11
	Multiple	2	10.53	4	21.05
No		10	52.63	7	36.84
Total		19	100.00	19	100.00

Table 14: Showing Outcome in Both Group

Outcome	Pinak(n=19)		Control(n=19)	
	Frequency	%	Frequency	%
Recovery	19	100.00	16	84.21
Death	0	0.00	3	15.79
Total	19	100.00	19	100.00

3 Deaths are in patients with multiple co morbidities.

Table 15: Showing Ventilatory Time and Indoor Days in Both Groups

Outcome Patient Number	Ventilatory Time (days)		Indoor Stay (Days)	
	Pinak Group	Control Group	Pinak Group	Control Group
1	02	07	17	27
2	05	27	10	27
3	11	09	15	09
4	03	00	12	25
5	02	10	08	10
6	10	07	19	14
7	03	08	18	08
8	02	19	16	20
9	04	22	10	23
10	00	10	07	12
11	07	08	13	16
12	01	11	16	14
13	01	12	09	15
14	03	10	11	11
15	08	20	13	21
16	02	10	10	14
17	06	15	11	16
18	03	09	18	11
19	01	19	23	19

RED are DEATHS

Table 16: Showing Significance for Ventilator Time and Indoor Stay in Days

Parameter	Pinak(n=19)	Control(n=19)	t	P
Ventilatory time	3.89(3.1)	12.53(6.4)	1.71	< 0.01*
IndoorStay	13.47(4.3)	16.42(6.0)	1.69	< 0.05**

* Highly Significant

** Significant

Table 17: Showing Complications in Moderately Severe Group

Complications	Pinak Group Moderately Severe	Control Group Moderately Severe	Total
Acute Renal failure	1 (5.26%)	2 (10.52%)	3
Dialysis	0	2 (10.52%)	2
DIC	0	0	0
Cardiac complication	0	2 (10.52)	2
Surgical intervention/Tracheostomy	0	1 (5.26%)	1
Ventilatory assistance/ O2 mean Duration	3.89 Days, SD= ± 3.1	12.53 Days SD= ± 6.4	--

Death	0	3 (15.78%)	3
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Table 18: Showing Outcome of the Patients of Moderately Severe Category

	Pinak Study Group (n = 19)			Control Group (n = 19)		
	Discharged	Transferred to Non Covid ICU/Ward	Death	Discharged	Transferred to Non Covid ICU/Ward	Death
Number	15	2 (ICU), 2 ward	0	10	2 (ICU), 4 ward	3
Total	15 (79%)	4 (21%)	0 (0%)	10 (52.6%)	6 (31.6%)	3 (15.8%)

DISCUSSION:

In Ayurveda, **poisons** include all types of poisons including snake bite, scorpion stings, bee bites and all **viral infections**. Hence, we studied the structure of Covid 19. Most viruses are proteins only. And all CORONA viruses (HSV, HIV, SWINE FLUE, COVID 19 etc.) attach to host cells by their 'S' Glycoprotein in the form of spikes. **COVID 19 has S protein spikes; hence Pinak will make it ineffective by breaking S Glycoprotein. Hence, we did add on treatment trial at Smt. Kashibai Navale Medical College and General Hospital on COVID 19 patients.**

IN MILD SYMPTOMATIC GROUP:

- Table number 1 shows No statistical significant difference was found in Control & Pinak groups in relation to age and sex. Maximum patients are from the age group 30 – 45 years (30% - 42.11%)
- About 40% patients are Asymptomatic as seen in table number 2.
- Prominent symptoms noted are like URTI. It includes running nose, sore throat and cough as seen in table numbers 2.1.
- As in table number 2.1 and table number 2.2, Cough, sore throat (87.5%) and fever (68.75%) are common symptoms.
- Laboratory investigations (table no. 5) and X ray chest of most of the mild patients were normal.
- Table number 5 shows Effect of drug Pinak on **symptomatic relief** is **STATISTICALLY SIGNIFICANT**.
($t = -5.29$, $p = <0.01$) In Pinak study group, symptomatic relief is seen in 3.14 days while Control group showed symptomatic relief in 6.39 days.
- Early symptomatic relief** is obtained due to tablet **Pinak** in **3.14 days** ($SD = \pm 1.8$), $t = -$

5.29, $p < 0.01$) as seen from Graph number 1, Graph number 2 and table numbers 6th, 7th, 8th.

- There is **significantly early recovery** in patients who had taken Pinak on **3rd day in 72.73%**, on **5th day in 95.45%** and on **7th day in 100%** patients. Control group showed relief on 3rd day in **11%**, on 5th day in **39%** and on 7th day in **61%** patients. See Graph no.1, Graph no. 2 and table no. 8.
Early Recovery of patients due to Pinak leading to reduced Morbidity and Mortality is confirmed from tables 6, 7 & 8.
- Co – morbidities did not have much outcome significance in Mild Patients if treated with Pinak.** Study group has 26.32% and control group has 36.67% co morbid patients as in table number 3 & 13.
- Table no. 9 shows, after **5 days** of treatment, Swab testing was done in 8 patients. 4 patients were **NEGATIVE** while 4 patients tested **POSITIVE**.
- 3 out of 33 (9.09%)** patients who were admitted as mild patients from control group, needed ICU treatment as seen from table no. 10 confirming that Pinak reduces morbidity and hence mortality.

IN MODERATELY SEVERE GROUP:

- Table number 11 shows no statistical difference in age distribution.
- Control group has 78% males; while Pinak group has 52% females in table number 12.
- Co morbidities were 31.58% in moderately severe patients both in Study group and control group as seen in table number 13.
- Table number 18 shows Study group with **Pinak** in Moderately severe patients showed **100% Recovery**; while in **Control** group recovery rate is **84.2%**.
- Complications like Renal failure in 2 (10.52%), Cardiovascular complications in 2 (10.52%) Tracheostomy in 1 (5.26%) and

Dialysis in 2 (10.52%) were seen only in control group of moderately severe patients as seen from the table no 17.

17. **Cardiovascular** complications seen only in control group & not in Pinak study group.
18. **ARF** patients in Control group required **Haemodialysis**, but not in Pinak study group.
19. In Moderately severe group, 4 out of 19 (21%) patients from study group with Pinak needed additional medical treatment in **nonCovid ward**. While 6 out of 19 (31.6%) patients from control group needed additional medical treatment in non Covid ICU and ward as seen from table no 18.
20. Table no. 15 significantly shows that **Average Ventilatory time or O2 time** in study group with Pinak is **3.89 Days, SD= ± 3.1** While in control group it is **12.53 Days SD= ± 6.4**
 $t = 1.71, p = < 0.01$.
21. As Ventilatory time is reduced significantly, **Expenditure for ICU treatment is reduced** significantly by rupees one lack per patient.
22. Also due to **reduced ventilator time**, not a single patient required Tracheostomy.
23. Table no 15 also shows that **Average stay** of patients from moderately severe group is 13.47 (4.3) days in PINAK study group and 16.42(6.0) days in control group. $t = 1.69, p = < 0.05$.
24. Table number 16 shows **3 out of 19 (15.8%)** patients from moderately severe control group **died** on 8, 9 and 10th day. Nobody from study group with Pinak died.

LIMITATIONS:

1. Patients in Critical ICU on MV are not included in this study.
2. Intubated patients are not benefitted by Pinak. Tissue damage is more in such patients making life unsustainable.
3. Early treatment with Pinak benefits patients on Non Invasive Ventilation.

OTHER INFORMATION:

Ethical Committee approval was taken for that on 11-05-2020.

CTRI gave approval for the study on 23-05-2020 with No CTRI/2020/05/025326.

WE started enrolling patients for the study after the approval of Ethical Committee. CTRI suggested enrolling patients from 31st May. Later CTRI permitted to enroll admitted patients from 22nd May 2020.

SUMMARY AND CONCLUSION:

In our Add on study, 57 patients of Covid 19 received Pinak plus protocol drugs and control group of 49 patients received only protocol drugs. Following conclusions were found.

1. Pinak is **easy to administer**.
2. **EARLIER** is the institution of PINAK, **FASTER** is the Recovery.
3. **No adverse drug reaction** has been noticed during Pinak administration.
4. Pinak is **well tolerated and accepted** by patients.
5. **No significant drug interaction** with other allopathic drugs has been noticed during study.
6. Pinak **reduces time required to become symptom free**.
7. **Not a single patient from Pinak study group became hypoxic. Nobody required ICU care. Nobody required ventilator assistance.**
8. **Complications are minimal and of less severity** in Pinak group as compared to Control group.
9. **No deaths** were observed in patients with Pinak. Hence, death can be prevented with Pinak.
10. **Due to early recovery, significant economical saving in both Mild and Moderate & severe cases.**

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