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General Surgery

ROLE OF PIROXICAM IN CONTROLLING FEVER IN COVID 19 - AN OBSERVATIONAL CASE SERIES STUDY

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ABSTRACT **INTRODUCTION-** COVID 19 pandemic is creating havoc in medical infrastructure. Further misery is created by the fact that there is no proven treatment of COVID 19 infection. Most of the drugs given currently in COVID 19 is for symptomatic management of infection. Updated protocols released on time to time basis have drugs which are based more on clinical observations rather than experimental ones. These drugs consists mainly repositioned drugs already approved by FDA for other disease treatment.

METHOD- In our study, we have used Piroxicam polyhedral crystals sublingually for control of fever in COVID 19 pneumonia which was not controlled by Paracetamol and steroids combination. It was advised in patients progressing to severe disease category or developing pneumonia.

RESULT- Our case series with limited data shows that cases have responded well to Piroxicam in control of fever. They became normothermic after single dose of drug. Further, patients' blood oxygen levels have also improved with therapy; however, with limited data, a cause-effect relationship could not be determined.

CONCLUSION- At present, Piroxicam can be advised in COVID 19 infection under medical supervision for control of persistent high fever. In future, randomised studies are needed to further consolidate above claim that Piroxicam is helpful in controlling fever as well as improving blood oxygen saturation of cases.

KEYWORDS : Covid 19, Piroxicam, Pneumonia, Fever, Steroid

INTRODUCTION

Piroxicam is a drug which belongs to oxicam class of Non steroidal anti-inflammatory drugs (NSAIDs). It inhibits synthesis of prostaglandins in body. It acts on cyclooxygenase enzyme. Cyclooxygenase helps in synthesis of prostaglandins. Piroxicam is non selective cyclooxygenase inhibitor, since it inhibits both COX1 and COX2 enzymes. Therefore, it stalls conversion of arachidonic acid into its prostaglandin precursors. This step is important for its anti pyretic and analgesic effects. Piroxicam also inhibits activation of neutrophils which imparts anti inflammatory property. Piroxicam is metabolized in liver by hydroxylation and glucuronidation. It may lead to mild increase in aminotransferase levels. Half-life of Piroxicam is 14-158 hr (average 50 hr). Its onset of action in body is after 15-30 min and duration of action is for 48-72hr. Peak plasma value of drug is seen at 3-5 hr after a single 20 mg dose. 99.3% of drug is protein bound and excreted in urine and feces. Piroxicam is mainly used in treatment of arthritis.[1]

Most of the drugs used currently to relieve COVID19 infection are based on clinical observations rather than any experimental study. There were concerns that NSAID may cause adverse events in acute viral infections but none of the concern was found to be accurate.[2]

The half maximal cytotoxic concentration "CC50" as calculated by MTT assay of Piroxicam is 1795 μM. Piroxicam also exhibits a promising in vitro activity against NRC-03-nhCoV (8.21 μM) and have promising antiviral activities with a high selectivity index (218.64) for antiviral activity relative to cellular toxicity.[3]

COVID-19 is a critical threat to public health. There is no existing antiviral therapy currently approved for its treatment. Drug repositioning represents a good approach to recognize off label use of FDA approved drugs as therapeutic options in COVID 19 that are different from their conventional uses.

METHODS

In this case series, 11 cases were taken for observational study. Prior informed written consent was taken from cases for administration of Piroxicam explaining its adverse effects.

Aim of the case series was to use Piroxicam as repositioned drug in control of persistent fever in COVID 19 pneumonia.

In all cases, Piroxicam polyhedral crystals were prescribed as 20 mg sublingual tablet in once a daily dose (OD) for 5 days.

8 cases in this series had mild COVID 19 infection defined as upper respiratory tract symptoms without shortness of breath or hypoxia. 3 cases had severe COVID 19 infection defined as SpO_2< 90% on room air.

Piroxicam was prescribed when cases were already taking other symptomatic COVID 19 medications like steroids (Methyl prednisolone/Dexamethasone/Budesonide), paracetamol and antibiotic as required and still had persistent high fever. Combination of these medications varied on case to case basis.

INCLUSION CRITERIA- In our study, Piroxicam was given to all patients after day 5 of symptom onset. It was started in most patients on the basis of high fever which was not controlled by regular dose of oral paracetamol tablets and steroids.

Total duration of study was 20 days. All cases in series were treated during this time period only.

RESULTS

Observation of change in body temperature and oxygen saturation is tabulated below.

Table-1 – Effect of Piroxiacam Pre therapy and Post therapy on body temperature and blood oxygen level.

Age/ Sex	Comorbidities	Day of starting PIROXICAM	Pretherapy (SpO2,Temp.)	Temp & SpO_2 2 hr after taking Piroxicam	Avg. Temp & SpO_2 on Day 2 of Piroxicam	Avg. SpO2 and Temp. during therapy
33y/ M	Pre hypertensive	Day 7	95%, 104°F	97%, 98.1°F	98%, 98.0°F	98%, 97.9°F
35y/F	-	Day 6	96%, 102.8°F	98%, 97.7°F	99%, 98.1°F	98%, 98.2°F
58y/ F	Controlled DM, HTN and Obesity	Day 6	98%, 102.8°F	98%, 98.4°F	98%, 98.3°F	98%, 97.7°F
60y/ M	Controlled DM, HTN	Day 7	95%, 103.8°F	99%, 97.9°F	97%, 98.2°F	98%, 96.6°F

29y/M	-	Day 6	96%, 103°F	99%, 98.6°F	99%, 97.7°F	99%, 98.2°F
52y/M	-	Day 9	85%on Oxygen, 100.0°F	90% on Oxygen, 97.4°F	94% on Oxygen, 97.4°F	97% on room air, 97.7°F
65y/M	Controlled DM	Day 6	94%, 104°F	98%, 98.1°F	99%, 98.O°F	99%, 98.3°F
38y/M	-	Day 7	80%, 99.5°F	86% on room air, 97.6°F	92% on room air, 97.9°F	94% on room air, 98.1°F
36y/M	-	Day 13	84% on high flow oxygen, 99.0°F	86% on high flow oxygen, 98.1°F	78% on bipap, 98.0°F	80% on bipap, 98.1°F
68y/F	Controlled HTN	Day 6	92%, 101.7°F	98%, 97.6°F	99%, 98.1°F	97%, 98.2°F
47y/M	Controlled HTN	Day 6	93%, 102.4°F	98%, 98.2°F	99%, 97.7°F	99%, 97.5°F

M= MALE, F= FEMALE, DM= DIABETES MELLITUS, HTN= HYPERTENSION, TEMP= BODY TEMPERATURE

Out of 11 cases, 8 cases had persistent high fever and 3 cases had mild fever at the start of Piroxicam therapy. Patients were already on steroids and paracetamol. On reading 2 hours after taking Piroxicam, cases became normothermic. Day 2 of Piroxicam therapy had average normothermic temperature. Same trend of normothermic temperature was seen throughout the course of Piroxicam therapy.

Another aspect noted during Piroxicam therapy was improvement in average blood oxygen saturation (SpO_2) of cases.

DISCUSSION

As seen in series, Piroxicam was excellent in controlling fever which were uncontrolled by Paracetamol and steroids. In most cases, Piroxicam was advised on after day 5 of symptom onset. In clinical course of COVID 19 pneumonia, there is a window period of 5-7 days from diagnosis to development of MODS. Most of the patients recover after this window period and about 20% of patients progress to severe pneumonia which is characterized by high fever, decrease in oxygen saturation etc.[4] Piroxicam seems to be working on these patients who are progressing to MODS.

Further, in above data, there was improvement in oxygen saturation of patients who were taking Piroxicam. It may be attributed to Piroxicam or it can be a mere coincidence which needs further studies.

In most cases, Piroxicam is taken along with other combination drug such as steroids. Steroids have anti inflammatory and anti pyretic action which can lead to decrease in body temperature. But, in our series, patient was already on steroid and still had persistent fever. So, it can be inferred that decrease in temperature is due to Piroxicam. This requires further randomized studies. Since, COVID 19 infection is creating havoc and there is no proven therapy at present, repositioned drugs can be critical in saving many lives. Piroxicam can be tried under medical supervision in cases which are progressing to MODS or increasing in severity with persistent fever.

CONCLUSION

Piroxicam is a repositioned drug tried in cases of COVID 19 infection which were progressing to severe category. In our study, patients have shown improvement in fever and blood oxygen level after taking this drug. Since, data available is limited, further studies are required to prove its efficacy in COVID 19.

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