1. INTRODUCTION

Fever is perhaps the most common manifestation of ill health due to infection[1]. It is an early and non- specific body response to many infectious and non-infectious causes. Fever implies an elevated core body temperature of more than 38.0^0c. Fever is a response to cytokines and acute phase proteins[2] . Fever is the most common presenting symptom of a varied group of disease. Fever is a complex pathological process that manifests itself as a regulated elevation of body temperature over the normal circadian variations. Although fever may be regarded as a host defence response, it has potentially harmful consequences such as convulsions, dehydration, especially brain damage and seizures usually happen during severe and long-lasting fever in children . Therefore, quite a number of people think that fever is a disease rather than a symptom or sign of illness and it is important to keep the body temperature in the state of homeostasis within the narrow range. As a thermoregulatory manifestation to systemic inflammation, fever has been studied for years[3].

Body temperature is controlled by hypothalamus .A normal body temperature is ordinarily maintained , despite environmental variations, because the hypothalamic thermoregulatory center balances the excess heat production derived from metabolic activity in muscles and the liver with heat dissipation from the skin and the lungs[4] . The normal diurinal variation is 1^0F the normal body temperature is more towards evening because of increased BMR and increased skeletal muscle activity[5].

Homoeopathic medicine Arsenicum album is selected for this study. It is one of the anti-pyretic remedy[6]. Arsenicum album is one of the most frequently used

homeopathic remedies and is one of the most well-proven remedies. A polychrest with a wide field of action, arsenicum album has the power to affect all parts of the human body. Its profoundly acting remedy on every organ and tissue its general symptoms often alone lead to its successful application mentally the patient is extremely nervous restless and anxious. Arsenicum album is mainly given for febrile attacks mostly in morning or evening, often with shivering and heat slightly developed.(7) it is one of the oldest of Hahnemann's provings but not published in fragments, nor in the first volume of his Materia Medica. Gastro intestinal inflammation is greater in degree. Toxic doses first elevate the temperature and then depress it. Medicinal doses reduce the temperature(8). Arsenic exhausts the vital power of certain organs or systems or of the entire organism, produces symptoms of impended activity in the functions of organs. Arsenicum is one of the best remedies for fevers of a typhoid character(9). Arsenic affects every part of man : it seems to exaggerate or depress almost all his faculties, to excite or disturb all his functions ; it has certain prevailing and striking features(10).

1.1 BACKGROUND AND JUSTIFICATION FOR THE STUDY:

From a retrospective study on Arsenicum album it is found that Arsenicum album has great affinity for intermittent fevers and chills. It is having anti parasitic action so hence it is used for malarial fever. parasitaemia of mice treated with Arsenicum album displayed irregular behaviour with a significant antimalarial effect on days 4 and 9, although less so on days 2, 3 and 5. Number of schizonts was always higher in the groups treated with Arsenicum album than in mice treated with vehicle or chloroquine .So it is

concluded from that experiment Arsenicum album had a significant inhibitory effect on parasitemia of mice infected with Plasmodium berghei.

In this modern era infectious disease and intermittent fevers are most common. So, I wish to prove experimentally the action of Arsenicum album for pyrexia in yeast induced albino rats.

SCOPE OF THE STUDY

- This is an evidence based study.
- there are not much of experimental studies in homoeopathy. this becomes one of the experimental studies in homoeopathy.
- authenticity of homoeopathic materia medica can be experimentally proved.
- this becomes an experimental model for conducting study on other drugs.
- notion of the current scientific world and laymen about homoeopathic research can be changed.
- proves that second phase pharmaceutical trials are possible in homoeopathy.
- acceptance by scientific community
- gives courage to budding homoeopaths to take up animal experiments.

2 AIMS AND OBJECTIVES:

- To study the effect of ARSENICUM ALBUM for pyrexia in baker's yeast incuced albino rats.
- To compare the effect of ARSENICUM ALBUM with paracetmol in controlling pyrexia.

3 **REVIEW OF LITERATURE**

DEFINITION

It is an elevation of body temperature above the normal circadian variation as a result of change in the thermoregulatory centre, located in the hypothalamus.(11) Body temperature is controlled by the thermoregulatory centre in the anterior hypothalamus in the floor of third ventricle(12). In healthy individual , normal body temperature varies from 36.6 to 37.2^{0}C , usually 98.4^{0}F . Body temperature between 99^{0}F and 105^{0}F and onwards is called pyrexia, while rise of body temperature above 107^{0}F is called hyperpyrexia.(13)

- HYPERTHERMIA: It refers to extreme elevation of temperature above 41^{0}C (106^0 F)It could be due to heat stroke, heat exhaustion or malignant hyperpyrexia.
- HYPOTHERMIA: It refers to abnormally low temperature below 35^{0}C(95^{0}F) rectally(14).

Physiological response due to pyrexia

- Metabolism increases
- Blood pressure pulse rate and cardiac output increases
- Rate of respiration increases
- There occurs negative nitrogen balance
- There occurs dehydration and fall of plasma chloride level(15)

ETIOLOGY:

INFECTIONS

- BACTERIAL INFECTION:

Enteric fever, tuberculosis, UTI, infective endocarditis, rheumatic fever, chronic biliary tract infection, chronic recurrent bacteremias

- VIRAL INFECTIONS:

  Infectious mononucleosis and CMV infection

- FUNGAL INFECTIONS:

  Histoplasmosis and cryptococcosis

- CONNECTIVE TISSUE DISEASES:

  SLE, Rheumatoid arthritis, rheumatic fever, polyarteritis nodosa, temporal artertis

- OTHER INFECTIONS:

  Infective endocarditis , brucellosis, osteomyelitis, dental and sinus infections ,

  Enteric fever, malaria, amebiasis, syphilis, leprosy, leishmaniasis and prostatitis.

- HORMONAL IMBALANCE
- MALIGNANCY:

  Leukaemia, lymphomas, and multiple myeloma, Solid tumors like renal cell carcinoma, liver, colon, stomach, pancreatic cancers

- DISEASES OF THYROID:

  Hypothyroidism, Hyperthyroidism, Hashimotos thyroiditis .

- AUTOIMMUNE DISEASE:

  SLE, rheumatoid arthritis, rheumatic fever, polyarteritis nodosa, temporal arteritis

  Polymyalgia rheumatic.(16)

- OTHERS:

- At the time of menstruation, Excessive labour, Sun stroke, Injury Hormonal imbalance

PATTERNS OF FEVER:

- CONTINUES FEVER:

  The temperature is elevated all the time but the difference between the maximum and minimum does not exceed 1°c.

- REMITTENT FEVER:

  The temperature is elevated through out but the fluctuation is more than 1°c

- INTERMITTENT FEVER :

  The temperature rises and falls , touching normal in between peaks

- PEL- EBSTEIN'S FEVER :

  This is cyclic fever in which fever lasting 3 to 10 days alternate with afebrile periods of the same duration (13).

PATHOGENISIS

Fever production has a positive effect on the course of infection. However for every 1^0c rise in temperature ,there is a 13% increase in resting metabolic rate and oxygen consumption(5). Fever therefore leads to increased energy requirements at a time when anorexia leads to decreased food intake (12). Pyrogens are substances causing fever. These may exogenous or endogenous. Exogenous pyrogens are molecules which interact with host cells to induce secretion of pyrogenic cytokines. Most of these are microbial products, microbial toxins or whole micro-organisms. Endogenous pyrogens are cytokines which are small molecular weight proteins most important being

interleukin.IL-1, IL-2, and tumour necrosis factor alpha. The synthesis and release of pyrogenic cytokines are induce production of the pyrogenic cytokines. Main source of pyrogenic cytokines are monocytes and macrophages, and to a lesser extent neutrophils and lymphocytes. Fever production has a positive effect on the course of infection. However, for every 1^0C

Pyrogenic cytokines stimulate production of prostaglandin- PGE_2 from arachidonic acid near the hypothalamic thermoregulatory centre. Arachidonic acid near the hypothalamic thermoregulatory centre. Arachidonic acid near the hypothalamic thermoregulatory centre. Arachidonic acid is released from cell membrane by the enzyme -phospholipase A2. PGE_2 raises the set point in the thermoregulatory centre .pyrogenic cytokines also induce production of PGE_2 in the periphery which is responsible for myalgia, arthralgia and malaise that accompany fever . Temperature is ultimately regulated in the hypothalamus. A trigger of the fever, called a pyroxene, causes release of prostaglandin E2 (PGE2). PGE2 in turn acts on the hypothalamus, which creates a systemic response in the body, causing heat-generating effects to match a new higher temperature set point.(4)

In many respects, the hypothalamus works like a thermostat. When the set point is raised, the body increases its temperature through both active generation of heat and retention of heat. Peripheral vasoconstriction both reduces heat loss through the skin and causes the person to feel cold. Nor epinephrine increases thermo genesis in brown adipose tissue, and muscle contraction through shivering raises the metabolic rate. If these measures are insufficient to make the blood temperature in the brain match the new set point in the hypothalamus,

then shivering begins in order to use muscle movements to produce more heat. When the hypothalamic set point moves back to baseline either spontaneously or with medication, the reverse of these processes (vasodilatation, end of shivering and no shivering heat production) and sweating are used to cool the body to the new, lower setting(17).

This contrasts with hyperthermia, in which the normal setting remains, and the body overheats through undesirable retention of excess heat or over-production of heat. Hyperthermia is usually the result of an excessively hot environment (heat stroke) or an adverse reaction to drugs. Fever can be differentiated from hyperthermia by the circumstances surrounding it and its response to anti-pyretic medications.(18)

PYROGEN:

A pyrogen is a substance that induces fever. These can be either internal (endogenous) or external (exogenous) to the body. The bacterial substance lip polysaccharide (LPS), present in the cell wall of gram-negative bacteria, is an example of an exogenous pyrogen. Pyrogenicity can vary: In extreme examples, some bacterial pyrogens known as superantigens can cause rapid and dangerous fevers. Depyrogenation may be achieved through filtration, distillation, chromatography, or inactivation(2).

In essence, all endogenous pyrogens are cytokines, molecules that are a part of the immune system. They are produced by activated immune cells and cause the increase in the thermoregulatory set point in the hypothalamus. Major endogenous pyrogens are interleukin 1 (α and β) and interleukin 6 (IL-6). Minor endogenous pyrogens include interleukin-8, tumor necrosis factor-β,

macrophage inflammatory protein-α and macrophage inflammatory protein-β as well as interferon-α, interferon-β, and interferon-γ. Tumor necrosis factor-α also acts as a pyrogen. It is mediated by interleukin 1 (IL-1) release

These cytokine factors are released into general circulation, where they migrate to the circumventricular organs of the brain due to easier absorption caused by the blood–brain barrier's reduced filtration action there. The cytokine factors then bind with endothelial receptors on vessel walls, or interact with local microglial cells. When these cytokine factors bind, the arachidonic acid pathway is then activated.

One model for the mechanism of fever caused by exogenous pyrogens includes LPS, which is a cell wall component of gram-negative bacteria. An immunological protein called lip polysaccharide-binding protein (LBP) binds to LPS. The LBP–LPS complex then binds to the CD14 receptor of a nearby macrophage. This binding results in the synthesis and release of various endogenous cytokine factors, such as interleukin 1 (IL-1), interleukin 6 (IL-6), and the tumor necrosis factor-alpha. In other words, exogenous factors cause release of endogenous factors, which, in turn, activate the arachidonic acid pathway. The highly toxic metabolism-boosting supplement 2,4-dinitrophenol induces high body temperature via the inhibition of ATP production by mitocho ndria, resulting in impairment of cellular respiration. Instead of producing ATP, the energy of the proton gradient is lost as heat.

PGE2 release comes from the arachidonic acid pathway. This pathway (as it relates to fever), is mediated by the enzymes phospholipase A2 (PLA2),

cyclooxygenase-2 (COX-2), and prostaglandin E2 synthase. These enzymes ultimately mediate the synthesis and release of PGE2.

PGE2 is the ultimate mediator of the febrile response. The set point temperature of the body will remain elevated until PGE2 is no longer present. PGE2 acts on neurons in the preoptic area (POA) through the prostaglandin E receptor 3 (EP3). EP3-expressing neurons in the POA innervate the dorsomedial hypothalamus , the rostral raphe pallidus nucleus in the medulla oblongata (rrpa), and the paraventricular nucleus of the hypothalamus . Fever signals sent to the dorsomedial hypothalamus and to the rostral raphe pallidus nucleus lead to stimulation of the sympathetic output system, which evokes non-shivering thermogenesis to produce body heat and skin vasoconstriction to decrease heat loss from the body surface. It is presumed that the innervation from the POA to the paraventricular nucleus mediates the neuroendocrine effects of fever through the pathway involving pituitary gland and various endocrine organs.(19)

CLINICAL FEATURES:

- High rise of temperature
- Headache
- Sensation of dullness in the body
- Dizziness
- Drowsiness
- Body ache
- Feeling cold and stiffness
- Sweating (20)

DIFFERENTIAL DIAGNOSIS:

- Malaria
- Chicken pox
- Typhoid fever (17)
- Pyrexia on unknown origin
- Pharyngitis
- Adenitis
- Dengue fever
- Pneumonia (21)

INVESTIGATIONS

- **Blood test:** routine blood count, hb, total wbc count, differential count, esr and peripheral smear study, c-reactive protein, biochemical profile, urea, electrolytes is to tested. A high leucocyte count is common in infections.
- Hb%, pcv, total count, platelet count.
- Urine routine and culture
- Creatinine
- Serological investigations-widal test, aso titre, hiv-elisa, vdrl, tpha, rheumatoid factor, antinuclear antibodies, viral antibody titres, paul-bunnell test, brucella agglutination test.
- Cpk-total
- examination of stool for diagnosing parasitic infecttions like malarial parasite
- Mantoux test to diagnosing tuberculosis
- Ast and alt(22)

- X-ray imaging: identify lessions in chest (eg; pneumonia and tuberculosis), paranasal sinuses, bones and joints.

GENERAL MANAGEMENT:

1. Tepid sponging to cool the skin-Alcohol sponges, cold sponges, ice bags, ice-water enemas and ice bath will lower the temperature.
2. Replacement of salt and water is important in patients with drenching sweat.
3. Maintain proper hand hygiene
4. Drink plenty of water as fever can cause cause fluid loss and dehydration(23)

MEDICINAL MANAGEMENT

arsenicum album

- Common name: white oxide of arsenic arsenic trioxide, white arsenic, white oxide of metallic arsenic, and arsenius acid
- Preparation: by separating arsenic from iron, cobalt or nickel by baking at high temperatures.

  Sphere of action:

  main seats of action of arsenic is mind, nerves, mucous membrane, joints , periosteum, liver , spleen, lymphatics, blood, lungs, skin, stomach, and alimentary canal. Arsenic acts more promptly on vegetarians than on non vegetarians(24).

  Pathogenesis:

  Arsenic is a poison and causes constant and violent irritation to all tissues such as

- Acting on gastro intestinal tract, it produces a picture like cholera asiatica.
- It attacks blood, causing septic changes ie, exanthemata, ecchymosis, petechial haemorrhage, etc
- It attacks veins, varices which burn like fire, especially at night.
- It attacks serous membrane causing copious serous effusion.
- It causes inflammatory swelling with burning lancinating pain.

  CONSTITUTION: the patient is lean, thin, debilitated having Hippocratic face, dirty and waxy look of skin. Very fastidious wants everything neat, clean and in order .
- Thermal:chilly patient
- Diathesis :scrophulous diathesis
- Miasm: psora, syphilis, **sycosis** (24)

Arsenicum album is a very deep acting remedy affecting every organ and tissue. This remedy derived from the metallic element arsenic(25). Traces of arsenic are found in vegetables and animals. In its crude form, arsenic is poisonous. Gradual accumulations may result in digestive disturbances, nausea, vomiting, diarrhea , dehydration, coma, shock, convulsions, paralysis, and death. Arsenicum Album is one of the fifteen most important remedies in homoeopathy. Arsenicum album persons are "tense, restless, ambitious individuals" with a tendency toward hypochondriasis , pessimism, need for reassurance , and a meticulous attention to neatness.(26) Arsenicum album has marked action on thermo regulation and very effective remedy for controlling fever. Febrile attack mostly in the morning or evening, often shivering and heat slightly developed. Cold over the whole body, sometimes with cold and viscid sweat. General coldness, with parchment like dryness of the skin or with profuse cold clammy perspiration. Shivering and shuddering.(27) Another important

characteristic is fear. The patient thinks it is useless to take medicine as his disease is incurable. The anxiety is caused by the real critical state of his sickness (28). Restlessness, nightly aggravation, great exhaustion after slightest exertion, burning which is relieved by heat(29). Periodicity of complaints is marked . Patient has midnight aggravation(30).

Mentally the patient is extremely nervous, restless and anxious(27). Physiological dose will produce vomiting, purging, and great prostration due to excessive secretion from gastrointestinal tract. It produces feeble pulse(24). Thirst is characteristic , with desire for frequent sips of water rather than a long drink. In fever may develop an unquenchable thirst quite large quantities during the sweating stage or in states of severe dehydration(24).

Arsenicum album is one of the best remedies for intermittent fevers and chills(9). Clarkes once treated some members of a family who all had attacks of f ever of short duration, recurring regularly every six weeks from living in rooms papered with arsenic nickel papers. Its periodicity comes every day, every 3^{rd} or 4^{th} day, every fortnight, every six week every year. Remedy for septic fevers and influenza. Body will be icy cold. It is prophylactic for yellow fever. Chill at night in bed, chill external and internal, worse from motion. Quartan, tertian shaking chill; periodicity marked; warm room does not ameliorate the chill. Fever afternoon and night; fever alternate with chill; fever and chill intermingled; dry, external heat; flushes of heat; chronic intermittent fever; internal heat with external coldness. Fever with no sweat and desire to uncover(31). Hectic fever with perspiration morning and night ; cold sweat, exhausting sweat , sweat on motion or on slight exertion profuse night sweat. Externally cold, with internal burning heat(27). Coldness in spots. Sensitive to

cold yet > in open air. Stool rice water, foul, small, involuntary, acrid, burning, black, mucous,< cold drinks, with much prostration (32).

MODALITIES:

AGGRAVATION:

Wet weather, after midnight, from cold, cold food and drinks, sea shore, right side.

AMELIORATION:

From heat, from head elevated, warm drinks(7).

COMPLIMENTARY : All-S, Carb v, Lach, Nat- S, Phos, Puls, Sulph, Thuja.

ANTIDOTES: Camphor, carbo veg, graphitis, china, hepar, ipecac.

RELATED ARTICLES

1)Experimental evaluation of antipyretic and analgesic activities of amalyakadi gana: An ayurvedic formulation(33).

2)In vivo evaluation of antipyretic effects of homoeopathic ultrahigh dilution of Typhoidinum on Baker's yeast induced fever in comparision with paracetamol(34).

3)Antipyretic activity of abutilon mauritianum (jacq) roots in wistar rats(35).

4. MATERIALS AND METHODS

4.1 STUDY SETTING:

This study was designed to evaluate the effectiveness of homoeopathy for pyrexia compare with paracetamol . The study was carried out by using18 female wistar albino rats . The rats are divided into 3 groups consisting of 6 animals each.

4.2 SELECTION OF SAMPLES

Healthy female albino rats of about 90 days old, weighing about 150-220g is taken for the study .

4.3STUDY DESIGN

This is an experimental study done on wistar albino rats with baker's yeast induced fever.

4. INTERVENTION

Arsenicum album 200 is administered orally by oral feeding needle for wistar albino rats. The remedy is given in water dose using distilled water that , 1 drop homoeopathic dilution arsenicum album 200 in 10 ml aqua five drops four hourly freshly prepared medicine is administered each time.

BRIEF OF PROCEDURES:

- Female wistar albino rats weighing about 150-220 g in the age group of about 90 days was acclimatized for the experimental room at

temperature 23+/- 2ºc, controlled humidity conditions (50-55%) and 12 hr light/dark cycle for a period of 1 week.

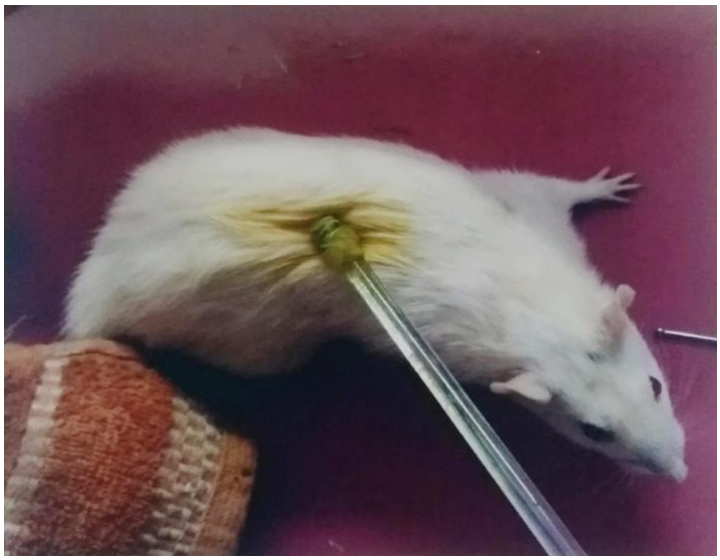
- Animals were caged with a maximum of 2 animals each in a polypropylene cage and fed with standard food pellets and water.
- After 1 week of acclimatization the animals were divided randomly into 3 groups, containing 6 animals each.
- Initially the Temperature of all the animals were noted rectally by using lubricated thermometer before inducing baker's yeast .
- Three groups of rats was treated with 135mg/kg baker's yeast (saccharomyces cerevisiae) suspended in 10 ml of normal saline was induced intraperitoneal for fever induction.
- Temperature was monitored rectally 4 hours after inducing bakers yeast by using lubricated thermometer
- The animal showing ≥0.5℉ f -1.5℉ raise of temperature were taken for the study
- Group1- receives vehicle (0.9% saline) orally and serves as control group.
- Group 2- orally treated with paracetamol 1mg/kg (Batch no: DOAS0108) 4 hourly by oral feeding needle
- Group 3- orally treated with Arsenicum album 200 (Dilution prepared from Dr Willmar Schwabe company batch no: 0252958) five drops four hourly by oral feeding needle. (1 drop homoeopathic dilution arsenicum album 200 in 10 ml of distilled water)
- Temperaure was monitored every hourly after the administration of drug

The blood sample were drained from the rat tail once before the administration of drug and 24 hours 48 hours after the administration of drug. And blood parameters such as total count, neutrophils , lymphocytes, Eosinophil, platelet count was analysed**.**

4.6 OUTCOME ASSESSMENT:

- Lubricated thermometer was used for measuring the temperature one hourly. and the temperature of group 1, group 2, group 3 was compared.

- The blood sample was drained from the rat tail once before the administration of drug and 24 hours 48 hours after the administration of drug. And blood parameters such as total wbc, neutrophils , lymphocytes, monocytes, platelet count, neutrophil lymphocyte ratio and monocyte –lymphocyte ratio was analysed**.**

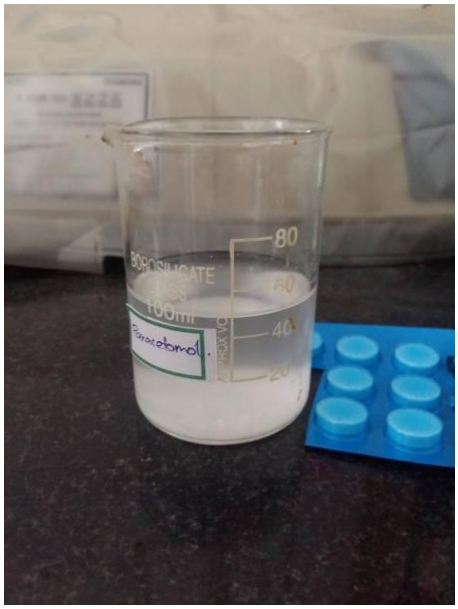
4.6.1)  GIVING IDENTIFICATION MARKS OF RATS

4.6.2) RATS IN CAGE WITH FOOD PELLETS AND WATER

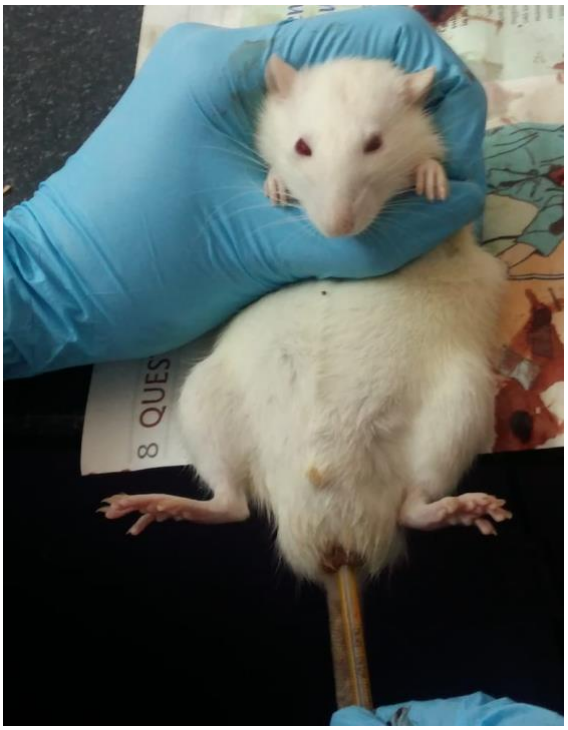
4.6.3) WEIGHING THE RATS

4.6.4) INJECTING BAKERS YEAST INTRAPERITONIAL

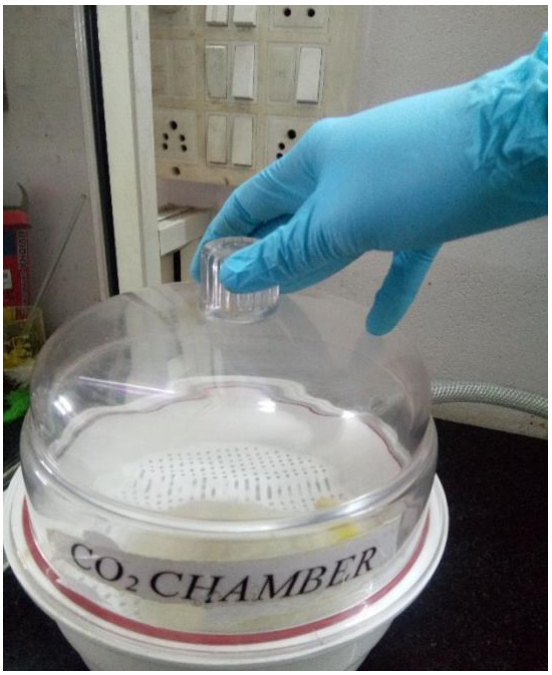
4.6.5) ADMINISTERING MEDICINE:



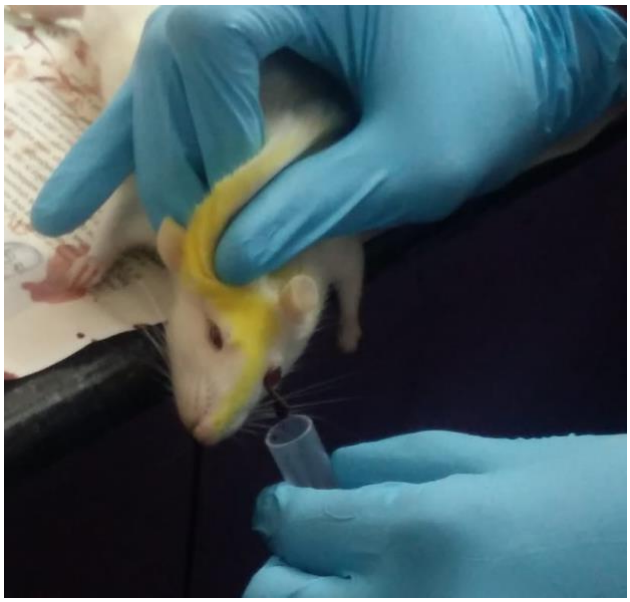
4.6.5) RECORDING OF TEMPERATURE



4.6.7) ANAESTHETIZING RATS



4.6.8) DRAWING BLOOD SAMPLE FROM ORBITAL SINUS OF RAT



5. OBSERVATIONS AND RESULTS

TABLE NO:1

MEAN TEMPERATURE OF GROUP 1- TREATED WITH SALINE

SL.NO	HOURS OF THE TEMPERATURE READING	MEAN TEMPERATURE OF GROUP 1
1	Initial temperture	98.43333
2	Before intervention	101.2365
3	1hr after intervention	103.5064
4	2hr	102.5999
5	3hr	102.3566
6	4hr	102.3594
7	5hr	100.8322
8	6hr	101.2279
9	7hr	101.3307
10	8hr	101.5651
11	12th hr	101.7977
12	16thhr	101.5645
13	20th hr	101.1658
14	24th hr	101.1566

CHART NO: 1

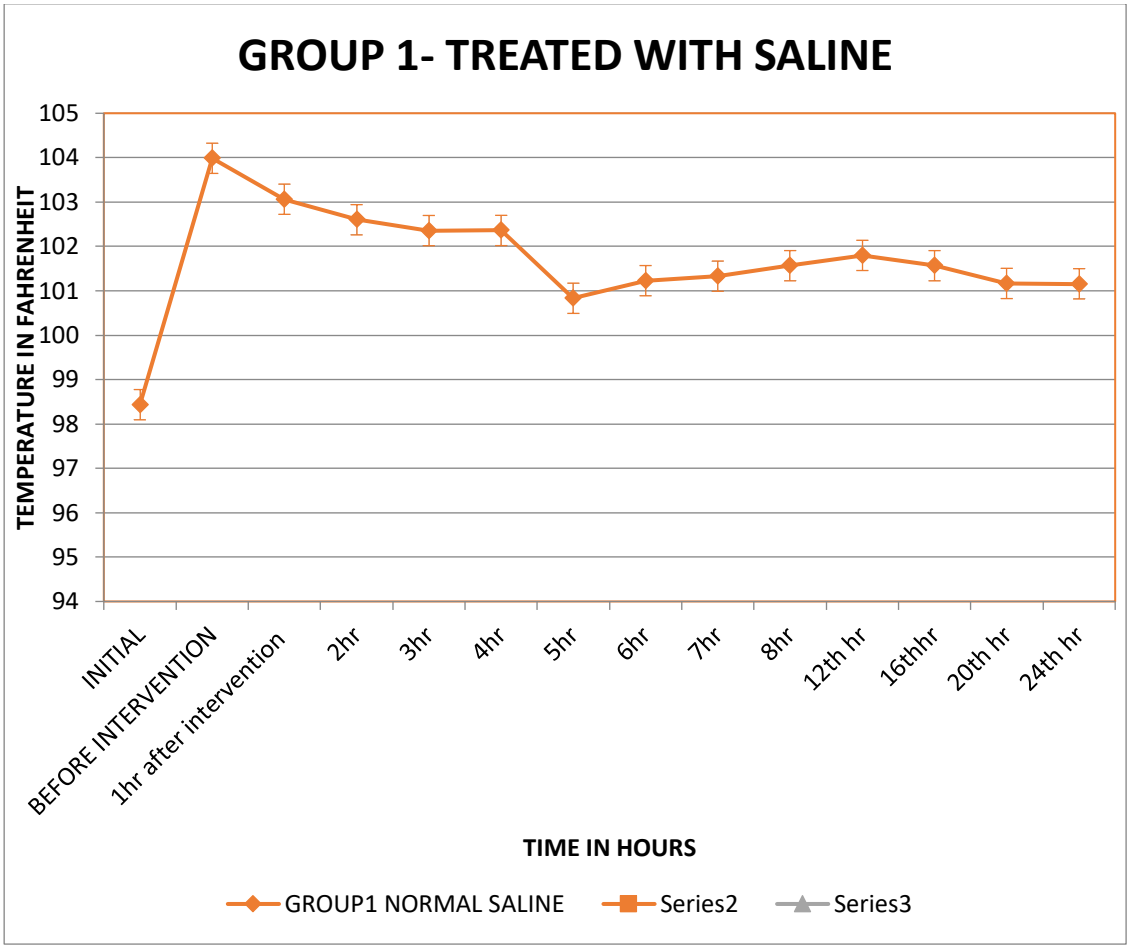

GROUP 1- TREATED WITH SALINE
TEMPERATURE IN FAHRENHEIT
105
104
103
102
101
100
99
98
97
96
95
94
INITIAL
BEFORE INTERVENTION
1hr after intervention
2hr
3hr
4hr
5hr
6hr
7hr
8hr
12th hr
16thhr
20th hr
24th hr
TIME IN HOURS
GROUP1 NORMAL SALINE
Series2
Series3

TABLE NO:2

MEAN TEMPERATURE OF GROUP 2-TREATED WITH PARACETOMOL

SL.NO	HOURS OF THE TEMPERATURE READING	MEAN TEMPERATURE OF GROUP 2
1.	INITIAL	97.63333
2.	BEFORE INTERVENTION	101.1964
3.	1hr AFTER INTERVENTION	99.931
4.	2hr	101.0979
5.	3hr	103.0299
6.	4hr	101.6323
7.	5hr	98.995
8.	6hr	100.7275
9.	7hr	100.7657
10.	8hr	100.4992
11.	12th hr	100.8995
12.	16thhr	100.6994
13.	20th hr	100.5639
14.	24th hr	100.3264

CHART NO: 2

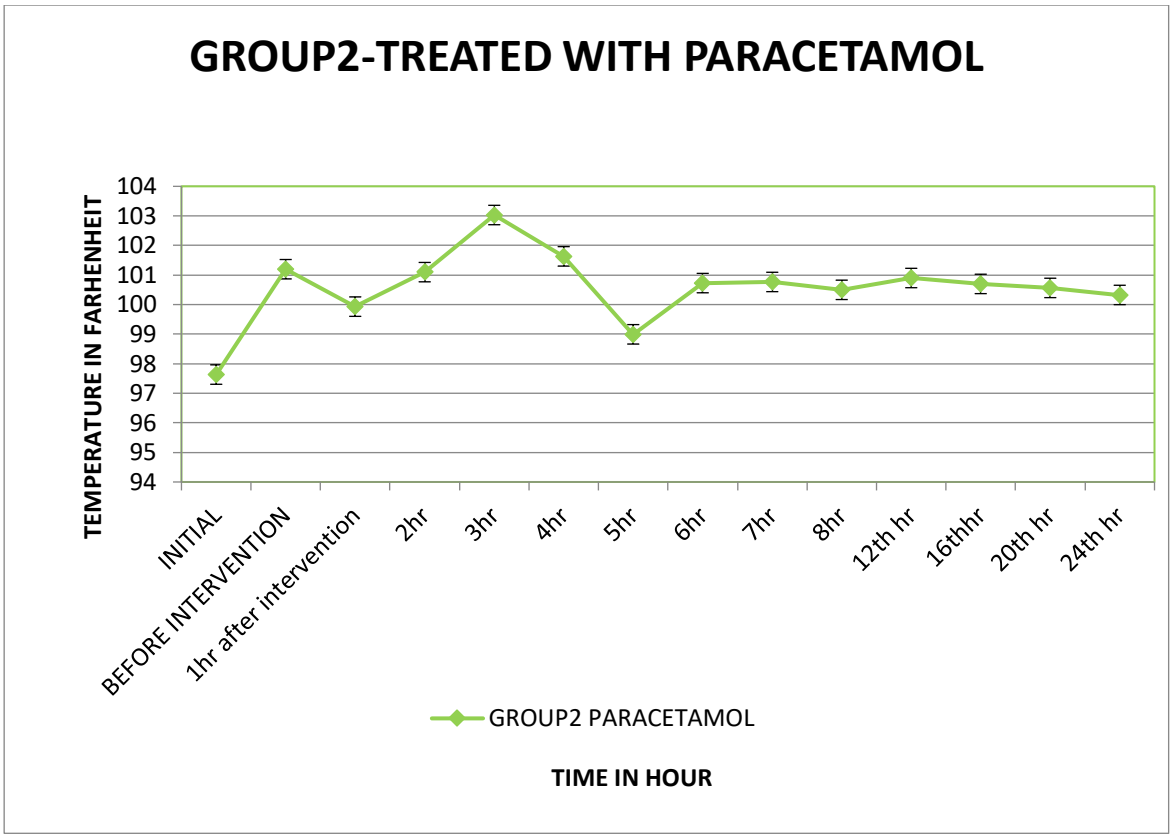

GROUP2-TREATED WITH PARACETAMOL
TEMPERATURE IN FARHENHEIT
104
103
102
101
100
99
98
97
96
95
94
INITIAL
BEFORE INTERVENTION
1hr after intervention
2hr
3hr
4hr
5hr
6hr
7hr
8hr
12th hr
16thhr
20th hr
24th hr
GROUP2 PARACETAMOL
TIME IN HOUR

TABLE NO:3

MEAN TEMPERATURE OF GROUP 2-TREATED WITH ARSENICUM ALBUM 200

SL.NO	HOURS OF THE TEMPERATURE READING	MEAN TEMPERATURE OF GROUP 2
1.	INITIAL	97.4325
2.	BEFORE INTERVENTION	101.2365
3.	1hr AFTER INTERVENTION	101.9317
4.	2hr	101.4983
5.	3hr	100.4283
6.	4hr	100.7905
7.	5hr	98.6528
8.	6hr	99.33148
9.	7hr	99.39662
10.	8hr	99.3975
11.	12^{th} hr	99.5721
12.	16^{th} hr	99.29928
13.	20^{th} hr	98.89975
14.	24^{th} hr	98.49914

CHART 3

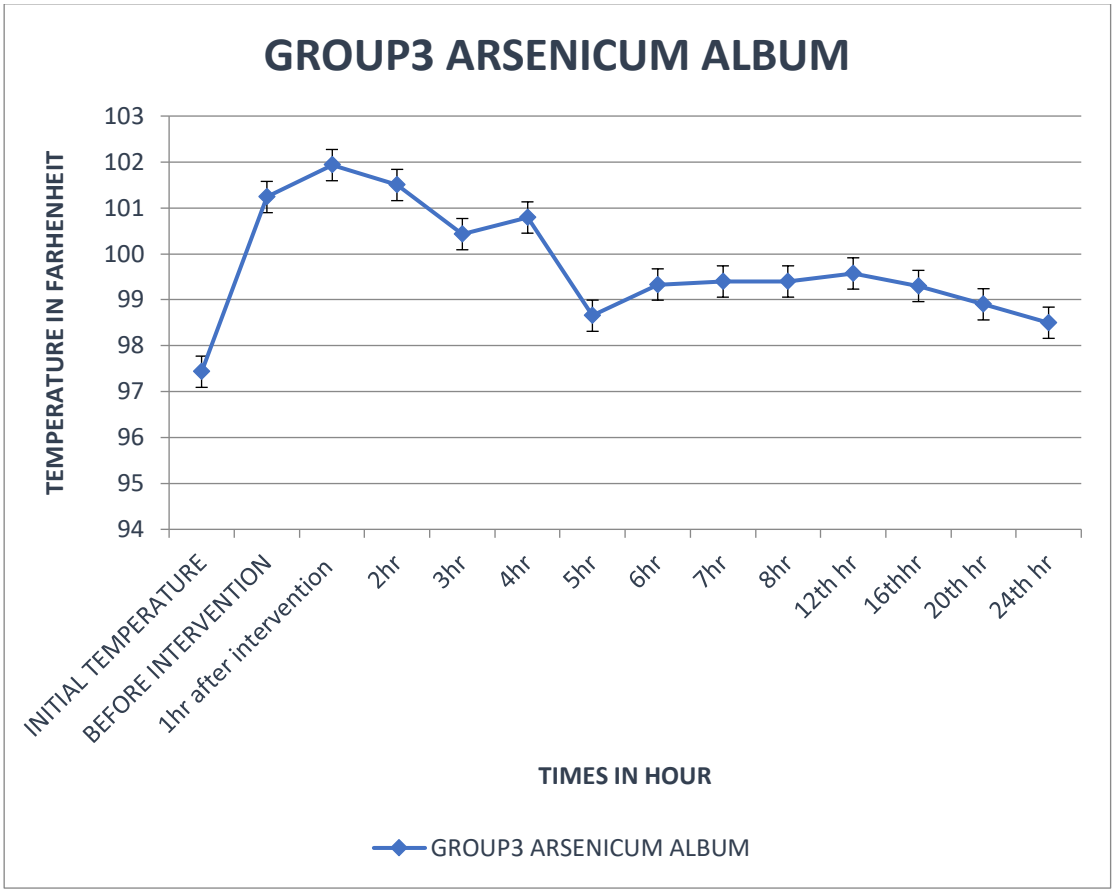

GROUP3 ARSENICUM ALBUM
TEMPERATURE IN FARHENHEIT
103
102
101
100
99
98
97
96
95
94
INITIAL TEMPERATURE
BEFORE INTERVENTION
1hr after intervention
2hr
3hr
4hr
5hr
6hr
7hr
8hr
12th hr
16thhr
20th hr
24th hr
TIMES IN HOUR
GROUP3 ARSENICUM ALBUM

TABLE NO :4

MEAN TEMPERATURE OF 3 GROUP

SL.NO	HOURS OF THE TEMPERATURE READING	MEAN TEMPERATURE		
		GROUP1	GROUP2	GROUP3
1.	INITIAL TEMPERATURE (BEFORE YEAST INDUCTION)	98.43333	97.63333	97.4325
2.	BEFORE INTERVENTION	103.9861	101.1964	101.2365
3.	1hr AFTER INTERVENTION	103.0643	99.931	101.9317
4.	2hr	102.5999	101.0979	101.4983
5.	3hr	102.3566	103.0299	100.4283
6.	4hr	102.3594	101.6323	100.7905
7.	5hr	100.8322	98.995	98.6528
8.	6hr	101.2279	100.7275	99.33148
9.	7hr	101.3307	100.7657	99.39662
10.	8hr	101.5651	100.4992	99.3975
11.	12^{th} hr	101.7977	100.8995	99.5721
12.	16^{th} hr	101.5645	100.6994	99.29928
13.	20^{th} hr	101.1658	100.5639	98.89975

CHART NO:4

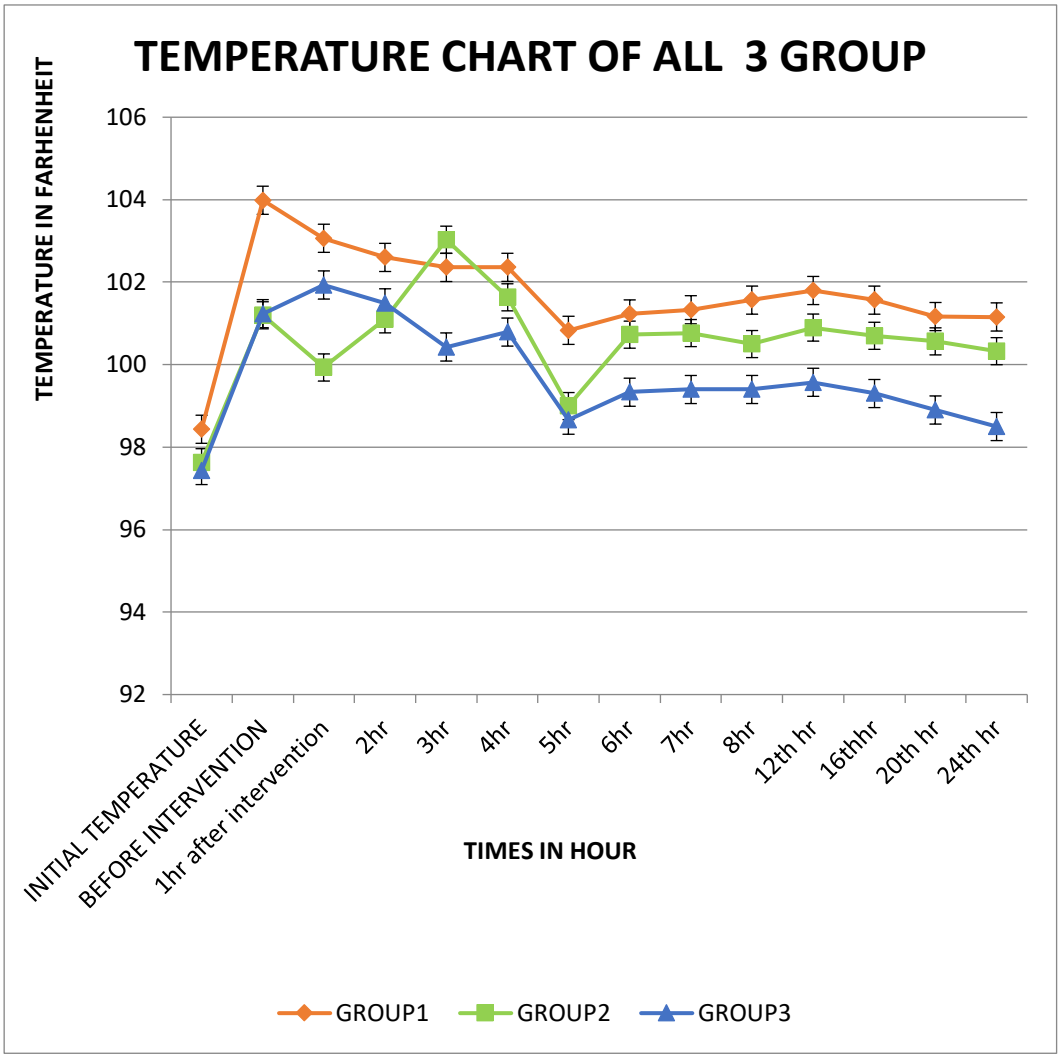

TEMPERATURE CHART OF ALL 3 GROUP
TEMPERATURE IN FARHENHEIT
106
104
102
100
98
96
94
92
INITIAL TEMPERATURE
BEFORE INTERVENTION
1hr after intervention
2hr
3hr
4hr
5hr
6hr
7hr
8hr
12th hr
16thhr
20th hr
24th hr
TIMES IN HOUR
GROUP1
GROUP2
GROUP3

TABLE NO:5

MEAN VALUE OF BLOOD PARAMETERS

BEFORE YEAST INDUCTION

SL..N0	GROUP	TC	PLATLETS	N	L	E
1	GROUP1	6416.667	27.83333	66.5	3.833333	683.3333
2	GROUP2	6866.667	29.83333	68.83333	2.166667	725
3	GROUP3	6600	29	63..33333	4.166667	650

CHART NO: 5

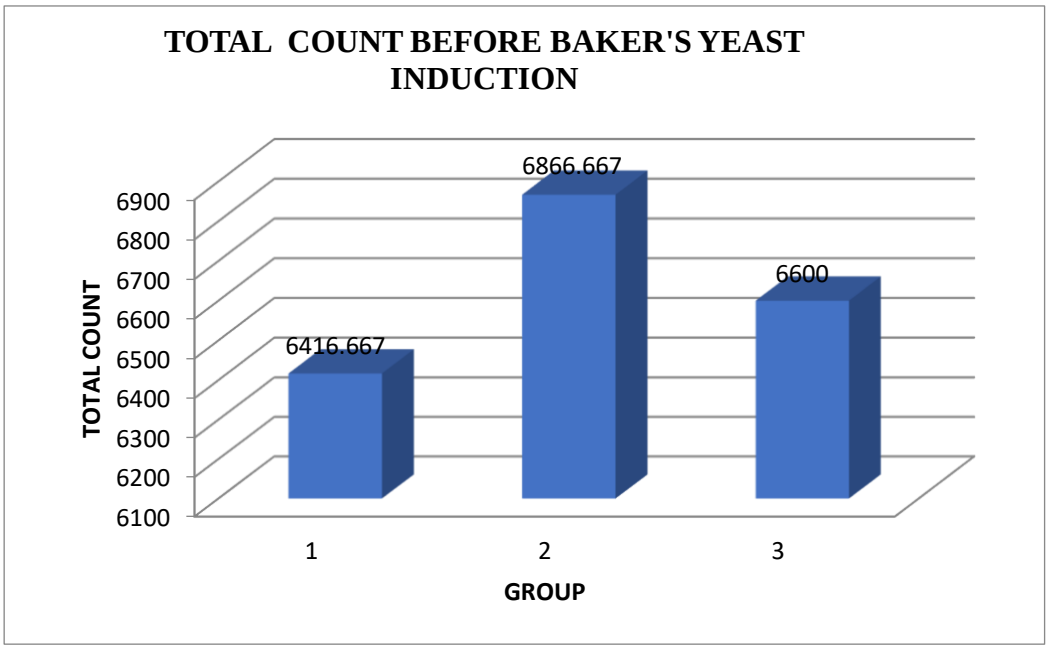


CHART NO: 6

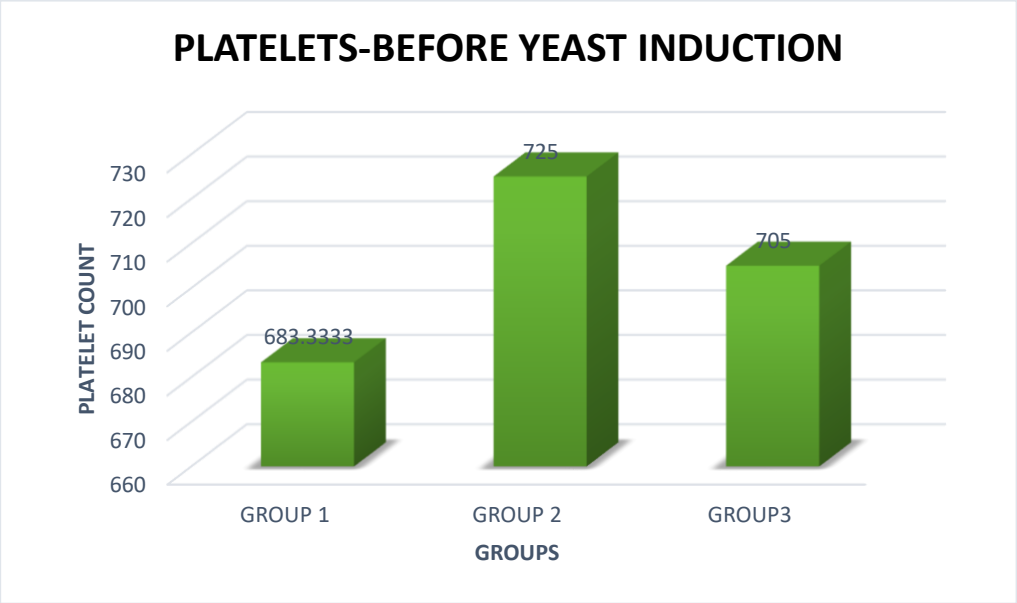


CHART NO:7

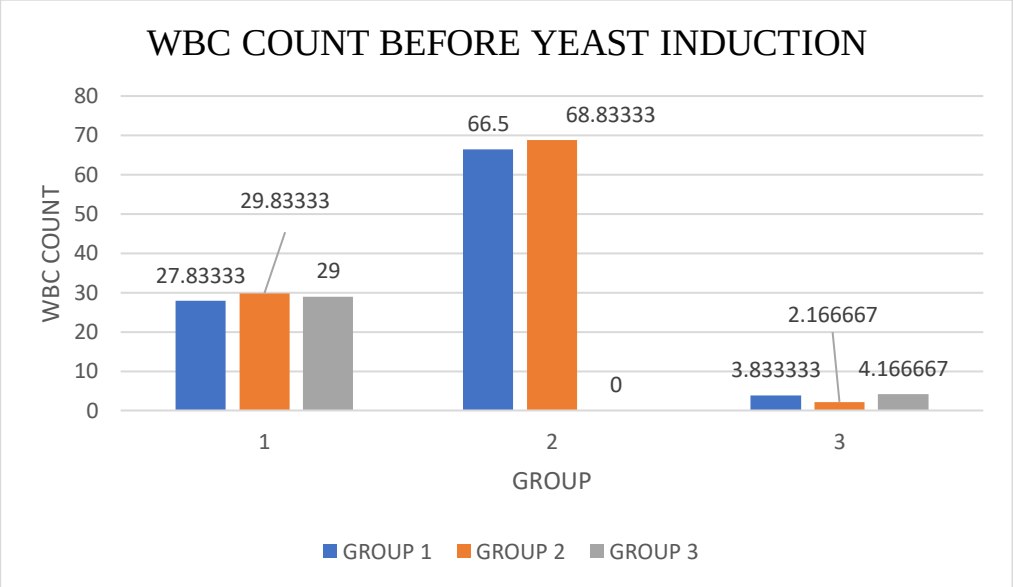


TABLE NO: 6

MEAN VALUE OF BLOOD PARAMETERS

AFTER YEAST INDUCTION

SL NO:	GROUP	TC	N	L	E	PLATLETS
1	GROUP1	6366.667	26	62	3.833333	620.8333
2	GROUP2	6100	24.16667	63.33333	3	641.6667
3	GROUP3	6033.333	26.33333	61.16667	3.833333	618.3333

CHART NO:8

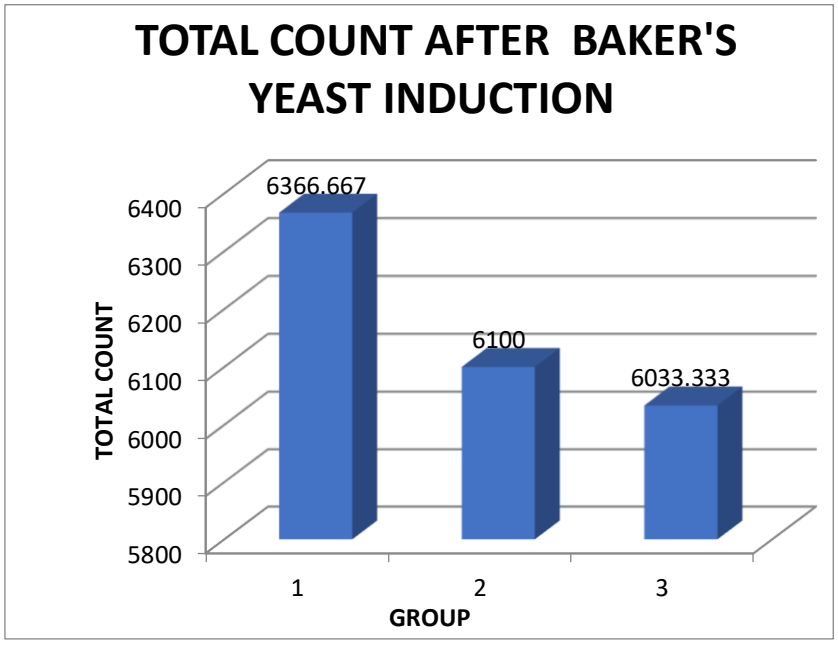


CHART NO:9

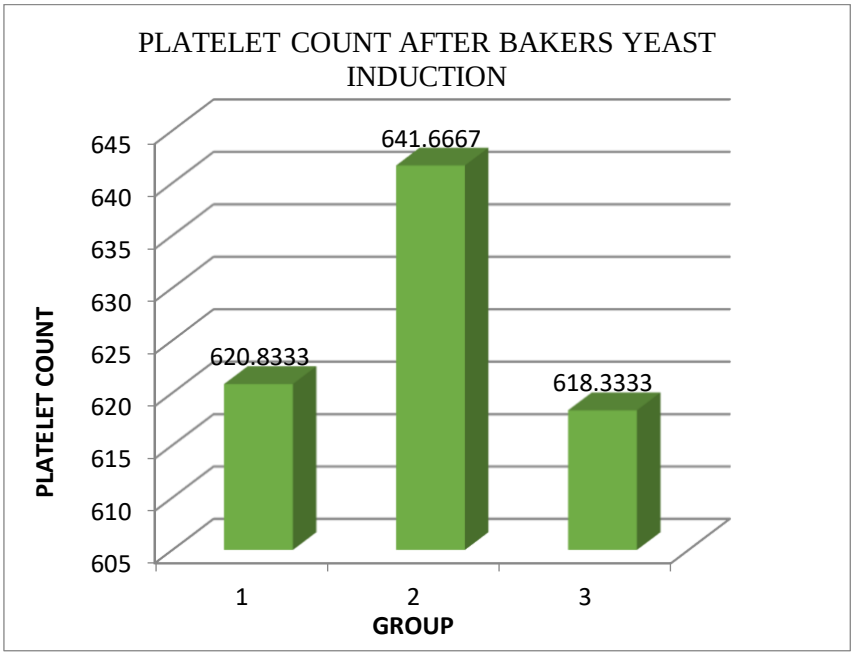


CHART NO:10

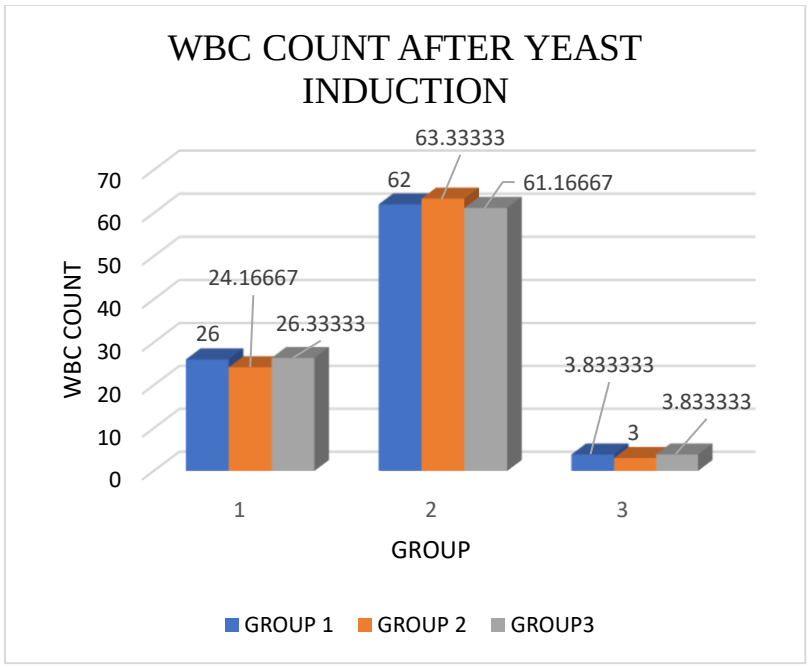


TABLE NO: 7

MEAN VALUE OF BLOOD PARAMETERS

AFTER INTERVENTION

SL.NO	GROUP	TC	PLATLETS	N	L	E
1	GROUP 1	6816.667	620.833	26	62	3
2	GROUP2	6583.333	641.6667	24.16667	61.66667	2.166667
3	GROUP3	6266.667	682.5	29	64.83333	2.166667

CHART NO 11

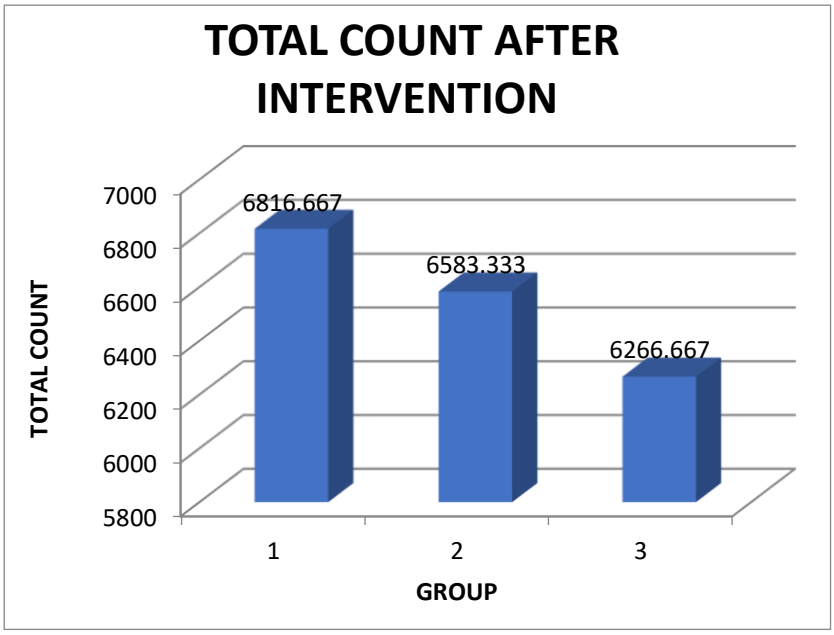


CHART NO 12

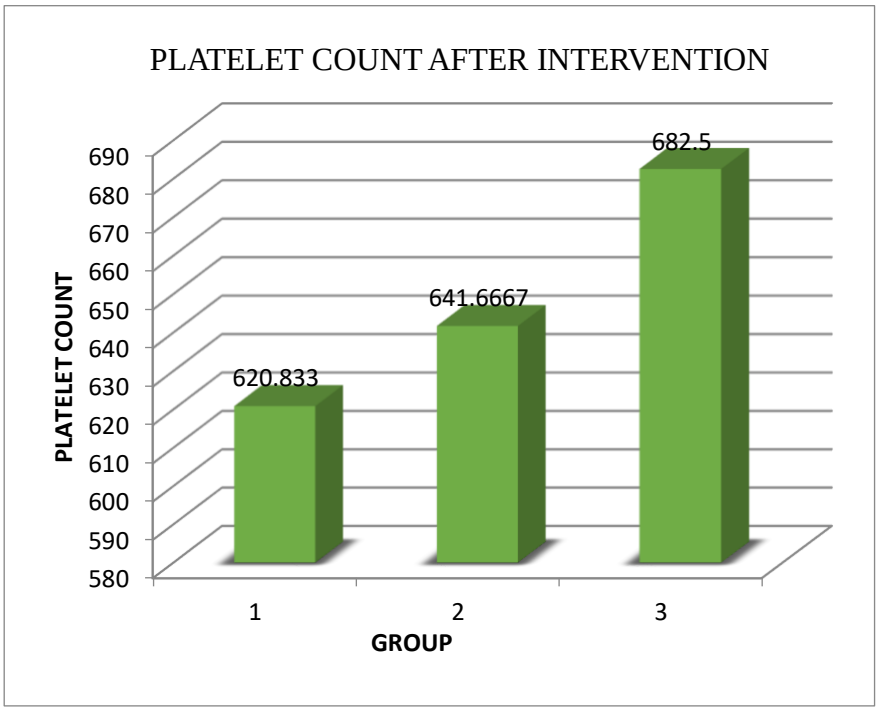


CHART NO: 13

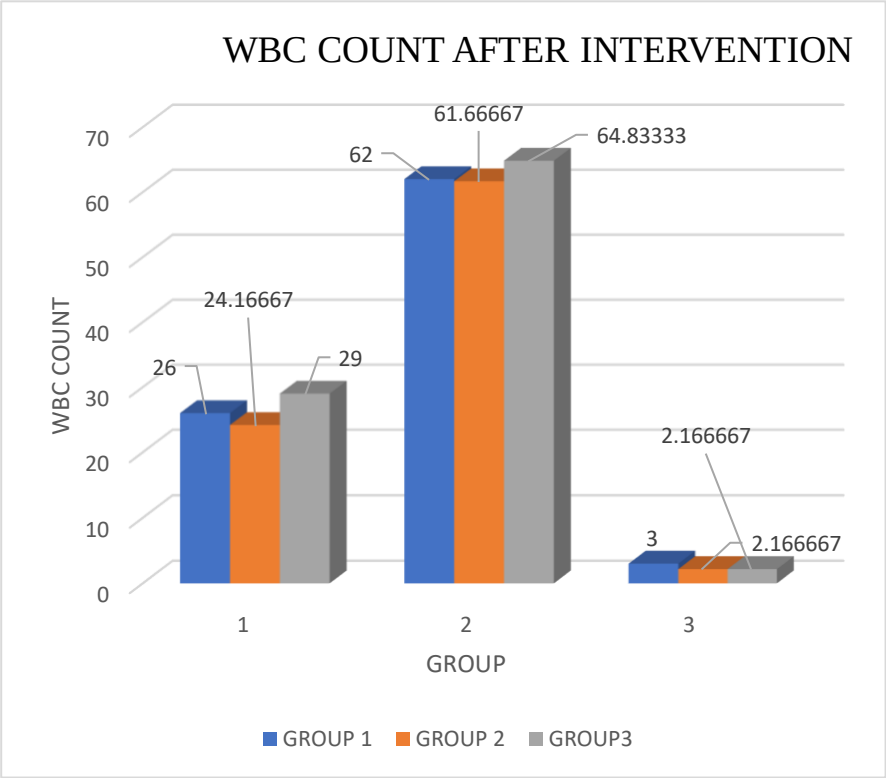


TABLE NO:8

MEAN VALUE OF BLOOD PARAMETERS

OF ALL THREE GROUP

BLOOD PARAMETERS	BEFORE YEAST INDUCTION			AFTER YEAST INDUCTION			AFTER INTERVENTION		
	G1	G2	G3	G1	G2	G3	G1	G2	G3
TOTAL COUNT	6416.667	6866.6	6600	6366.6	6100	6033.33	6816.6	6583.3	6266.6
PLATELETS	683.333	725	705	620.83	641.66	618.33	620.8	641.6	682.5
NEUTROPHIL	27.8333	29.833	29	26	24.166	26.333	26	24.166	29
LYMPHOCYTE	66.5	68.833	63.333	62	63.333	61.1666	62	61.666	64.83
EOSINOPHIL	3.8333	2.1666	4.1666	3.8333	3	3.833	3	2.1666	2.166

CHART NO:14

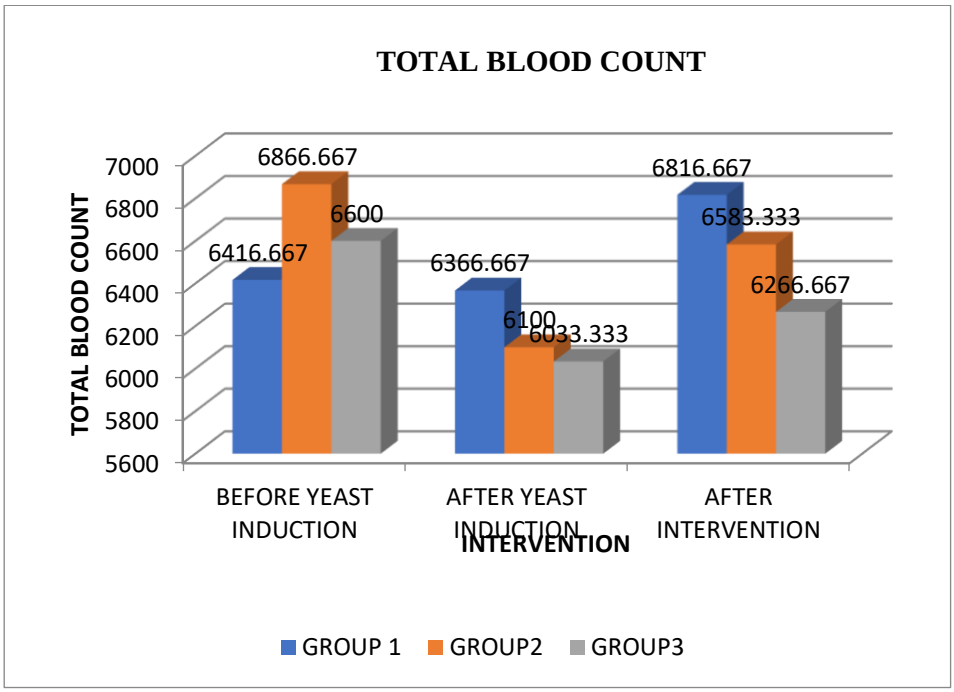

TOTAL BLOOD COUNT
TOTAL BLOOD COUNT
7000
6800
6600
6400
6200
6000
5800
5600
6866.667
6600
6416.667
6366.667
6100
6033.333
6816.667
6583.333
6266.667
BEFORE YEAST INDUCTION
AFTER YEAST INDUCTION
AFTER INTERVENTION
INTERVENTION
GROUP 1
GROUP2
GROUP3

CHART NO. 15

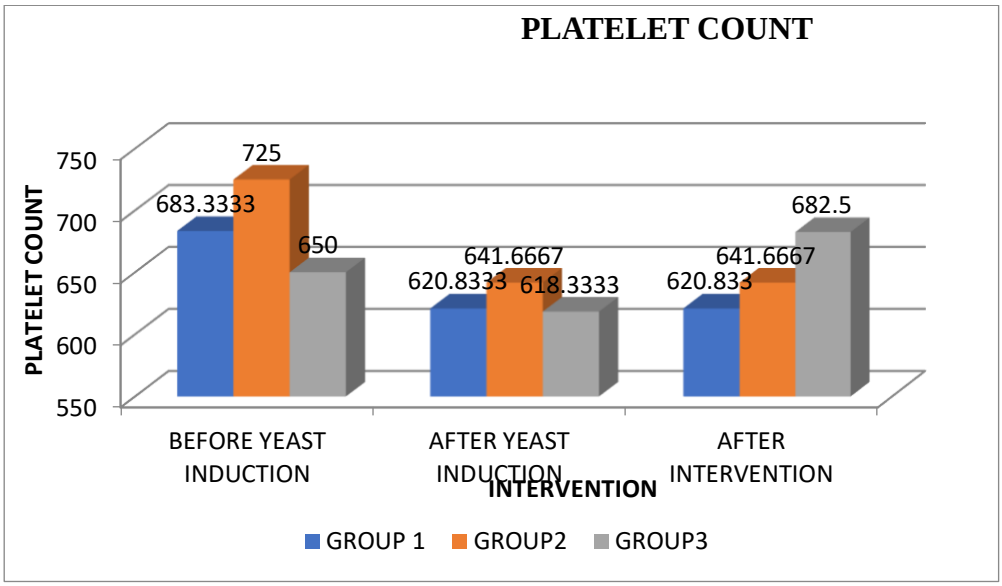

PLATELET COUNT
PLATELET COUNT
750
700
650
600
550
725
683.3333
650
641.6667
620.8333
618.3333
682.5
641.6667
620.833
BEFORE YEAST INDUCTION
AFTER YEAST INDUCTION
AFTER INTERVENTION
INTERVENTION
GROUP 1
GROUP2
GROUP3

CHART NO: 16

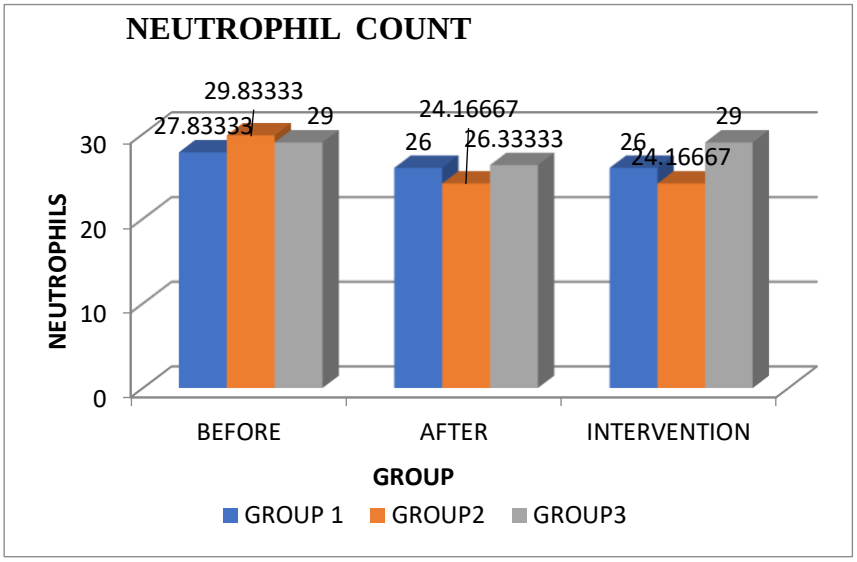

NEUTROPHIL COUNT
29.83333
27.83333
29
24.16667
26
26.33333
26
24.16667
29
30
20
10
0
NEUTROPHILS
BEFORE
AFTER
INTERVENTION
GROUP
GROUP 1
GROUP2
GROUP3

CHART NO. 17

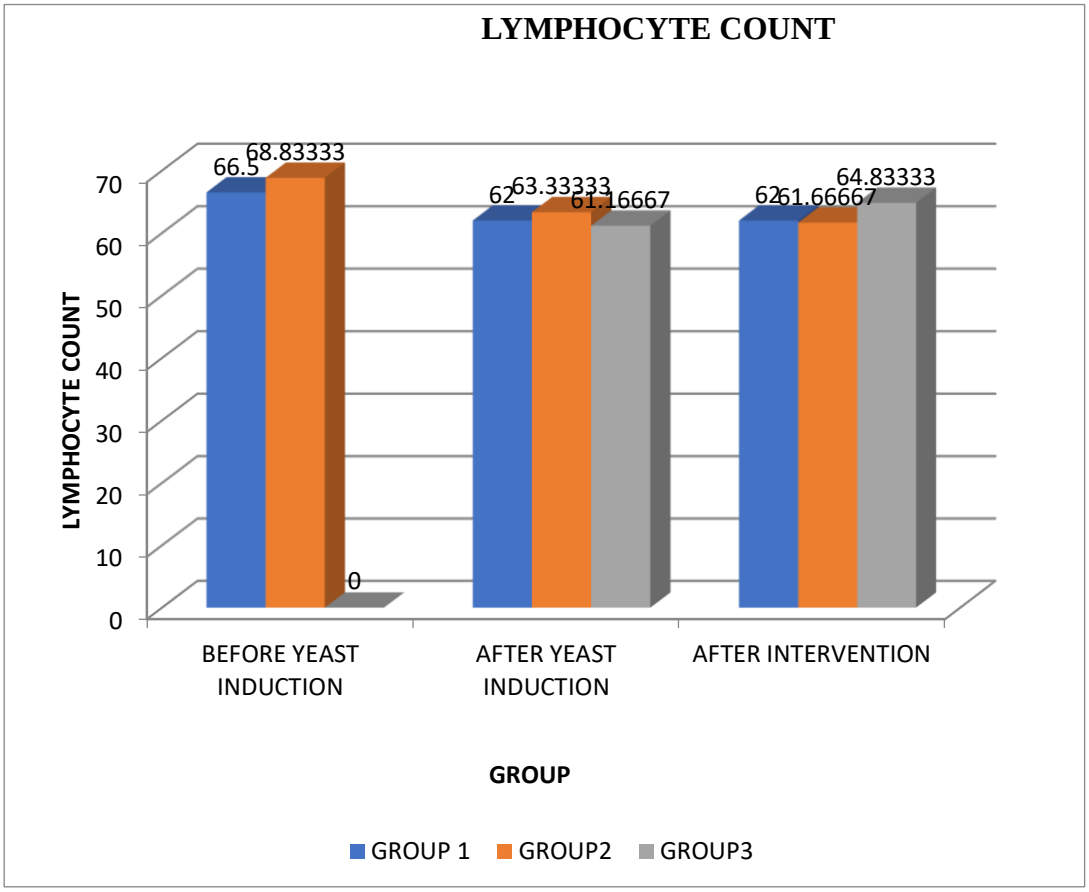
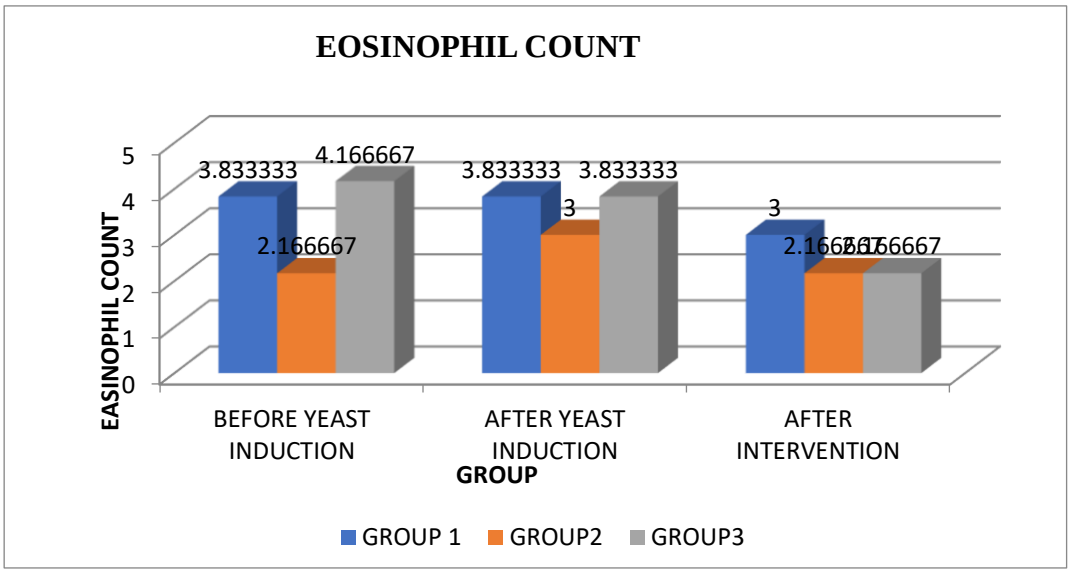

LYMPHOCYTE COUNT
LYMPHOCYTE COUNT
70
60
50
40
30
20
10
0
66.5
68.83333
0
62
63.33333
61.16667
62
61.66667
64.83333
BEFORE YEAST INDUCTION
AFTER YEAST INDUCTION
AFTER INTERVENTION
GROUP
GROUP 1
GROUP2
GROUP3

CHART NO. 18


EOSINOPHIL COUNT
EASINOPHIL COUNT
5
4
3
2
1
0
3.833333
4.166667
2.166667
3.833333
3.833333
3
3
2.166667
BEFORE YEAST INDUCTION
AFTER YEAST INDUCTION
AFTER INTERVENTION
GROUP
GROUP 1
GROUP2
GROUP3

5.1 OBSERVATION AND RESULT

From this study it can observe that the wonderful action of homoeopathic remedy Arsenicum Album. after the division of albino rats into 3 groups the temperature were monitered . the temperature is normal in all group before Baker's Yeast induction. After four hours of Baker's Yeast induction fever developed in all the rats. Every fourth hour intervention was given to three groups. Thereafter temperature was checked every one hourly until it become normal.

In Group1 after inducing bakers yeast temperature raises up to 101^0F and after intervention of Normal Saline it has increased to103^0F at first hour, then from second to fourth hour it has become 102^0F and on fifth hour it has become 100^0F and at sixth hour it reached 101^0F and remained constant till twentieth fourth hour.

In Group 2 after administering bakers yeast the temperature was at 101^0F and after intervention of Paracetamol it has reduced to 99^0F within first hour and increased to 101^0F at second hour and to 103^0F at third hour, then again after intervention of paracetamol at fourth hour it started to reducing and reached normal range that is 98^0F at fifth hour and from sixth hour onwards it increased to 100^0F and remained constant till twenty-fourth hour.

In Group 3 after administration of bakers yeast temperature was 101.2^0F . after intervention of Arsenicum Album at first hour it has increased to 101.9^0F and it has same after 2 hours then reduced to 100^0F at third hour and at fourth then fifth hour onwards the temperature become reduced gradually. sixth hour

onwards it comes to 99^0F and it constant for sixteenth hour then twentieth hour onwards it was 98^0F and remained constant till twenty-fourth hour.

Blood parameters also checked before Baker's Yeast induction, after Baker's Yeast induction and after intervention from orbital sinus of rat's eye to analyze the changes in blood parameters such as Total blood count, Platelet count, Neutrophil, Lymphocyte and Eosinophil count. Before Baker's Yeast induction the blood parameters showed a normal range. While, after Baker's Yeast induction blood parameters shows reduction in all the group.

When comparing the blood parameters after Baker's Yeast induction and after intervention it is observed that: Total blood count got slightly decreased in all group after bakers yeast induction and gradually increase to normal range after intervention. And in paracetamol group blood count remains same after intervention also. But in arsenicum album group the blood count become fall after bakers yeast induction then raised gradually and comes to normal except eosinophil count. and Platelets and lymphocyte count remained at the same level after intervention. In Group 1 treated with Normal Saline the lymphocyte count remained unchanged as before, while in Group 2 which was treated with Paracetamol showed a slight decrease in lymphocyte count and in Group 3 treated with Arsenicum Album 200 showed an increase in lymphocyte count. The Eosinophil count was decreased in all three group.

STATISTICAL ANALYSIS

ANALSIS OF BLOOD PARAMETRES

TOTAL COUNT

Source	**DF**	**Sum of Square (SS)**	**Mean Square (MS)**	**F Statistic (df_1, df_2)**	**P-value**
Intervention	2	369074.3815	184537.1907	3.4273 (2,4)	0.0058
Group	2	101666.8333	50833.4167	0.9441 (2,4)	0.0015
Error	4	215370.4074	53842.6019		
Total	**8**	**686111.6222**	**85763.9528**		

Among intervention since p-value > α, H0 can be rejected. The p-value equals 0.0058, ($p(x \leq 3.4273) = 0.8642$). The test statistic FA equals 3.4273, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value > α, H0 can be rejected. The p-value equals 0.0015, ($p(x \leq 0.9441) = 0.5385$). The test statistic FA equals 0.9441, which is in the 95% region of acceptance: [-∞: 6.9443]. Test is statistically significant.

PLATELET

Source	**DF**	**Sum of Square (SS)**	**Mean Square (MS)**	**F Statistic (df_1, df_2)**	**P-value**
Intervention	2	5385.3424	2692.6712	2.7566 (2,4)	0.0068
Group	2	1213.1293	606.5647	0.621 (2,4)	0.0023
Error	4	3907.2611	976.8153		
Total	**8**	**10505.7328**	**1313.2166**		

Among intervention Since p-value > α, H0 cannot be rejected. The p-value equals 0.0068, ($p(x \leq 2.7566) = 0.8232$. The test statistic FA equals 2.7566, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-

value > α, H0 cannot be rejected. The p-value equals 0.0023, (p(x≤0.621) = 0.4177). The test statistic FA equals 0.621, which is in the 95% region of acceptance: [-∞: 6.9443]. Test is statistically significant.

NEUTROPHIL

Source	**DF**	**Sum of Square (SS)**	**Mean Square (MS)**	**F Statistic (df_1, df_2)**	**P-value**
Intervention	2	18.5247	9.2623	3.7559 (2,4)	0.1207
Group	2	6.7839	3.392	1.3755 (2,4)	0.3511
Error	4	9.8642	2.466		
Total	**8**	**35.1728**	**4.3966**		

Among intervention Since p-value > α, H0 cannot be rejected. The p-value equals 0.1207, (p(x≤3.7559) = 0.8793). The test statistic FA equals 3.7559, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value > α, H0 cannot be rejected. The p-value equals 0.3511, (p(x≤1.3755) = 0.6489). The test statistic FA equals 1.3755, which is in the 95% region of acceptance: [-∞: 6.9443].

LYMPHOCYTE

Source	**DF**	**Sum of Square (SS)**	**Mean Square (MS)**	**F Statistic (df_1, df_2)**	**P-value**
Intervention	2	18.5247	9.2623	3.7559 (2,4)	0.1207
Group	2	6.7839	3.392	1.3755 (2,4)	0.3511
Error	4	9.8642	2.466		
Total	**8**	**35.1728**	**4.3966**		

Among intervention since p-value > α, H0 cannot be rejected.

The p-value equals 0.1207, (p(x≤3.7559) = 0.8793). The test statistic FA equals 3.7559, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value > α, H0 cannot be rejected. The p-value equals 0.3511, (p(x≤1.3755) = 0.6489). The test statistic FA equals 1.3755, which is in the 95% region of acceptance: [-∞: 6.9443].

EOSINOPHIL

Source	**DF**	**Sum of Square (SS)**	**Mean Square (MS)**	**F Statistic (df_1, df_2)**	**P-value**
Intervention	2	2.1543	1.0772	4.0347 (2,4)	0.1098
Group	2	2.1543	1.0772	4.0347 (2,4)	0.1098
Error	4	1.0679	0.267		
Total	**8**	**5.3765**	**0.6721**		

Among intervention Since p-value > α, H0 cannot be rejected. The p-value equals 0.1098, (p(x≤4.0347) = 0.8902). The test statistic FA equals 4.0347, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group Since p-value > α, H0 cannot be rejected.

The p-value equals 0.1098, (p(x≤4.0347) = 0.8902). The test statistic FA equals 4.0347, which is in the 95% region of acceptance: [-∞: 6.9443].

TEMPERATURE STATISTICS

Summary of Data

SOURCE	GROUP 1	GROUP 2	GROUP 3	TOTAL
N	14	14	14	42
∑X	1423.4401	1407.9974	1396.3665	4227.804
Mean	101.6743	100.5712	99.7405	100.662
$\sum X^2$	144748.436	141623.6709	139295.3259	425667.4328
Std.Dev.	1.2759	1.2284	1.2737	1.4669

Source	Ss	df	ms	
Between treatments	26.3509	2	13.1755	f=8.30527
When treatment	61.8695	39	1.5864	
Total	88.2205	41		

The *f*-ratio value is 8.30527. The *p*-value is .000989. The result is significant at $p < .05$.

Pairwise Comparisons		$HSD_{.05}$ = 1.1598 $HSD_{.01}$ = 1.4723	$Q_{.05}$ = 3.4455 $Q_{.01}$ = 4.3738
G_1:G_2	M_1 = 101.67 M_2 = 100.57	1.10	Q = 3.28 (p = .06515)
G_1:G_3	M_1 = 101.67 M_3 = 99.74	1.93	Q = 5.74 (p = .00065)

G_2:G_3	M_2 = 100.57 M_3 = 99.74	0.83	Q = 2.47 (p = .20167)

interpretation of statistics

Compared to control group and paracetamol group Homoeopathic remedy Arsenicum album200 has showed significant results with p value less than 0.05 and the f-ratio value is 8. 30527. after statistical analysis it can shows better action of homoeopathic remedy Arsenicum album 200 compared with paracetamol

In **Total Blood Count** Among intervention since p-value > α, H0 can be rejected. The p-value equals 0.0058, (p(x≤3.4273) = 0.8642). The test statistic FA equals 3.4273, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value > α, H0 cannot be rejected. The p-value equals 0.4615, (p(x≤0.9441) = 0.5385). The test statistic FA equals 0.9441, which is in the 95% region of acceptance: [-∞: 6.9443]. Test is statistically significant.

In **Platelet Count** Among intervention Since p-value > α, H0 can be rejected. The p-value equals 0.0068, (p(x≤2.7566) = 0.8232). The test statistic FA equals 2.7566, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value > α, H0 cannot be rejected. The p-value equals 0.5823, (p(x≤0.621) = 0.4177). The test statistic FA equals 0.621, which is in the 95% region of acceptance: [-∞: 6.9443].

So, it's statistically significant.

In **Neutrophil Count** Among intervention Since p-value > α, H0 cannot be rejected. The p-value equals 0.1207, (p(x≤3.7559) = 0.8793). The test statistic FA equals 3.7559, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value > α, H0 cannot be rejected. The p-value equals 0.3511, (p(x≤1.3755) = 0.6489). The test statistic FA equals 1.3755, which is in the 95% region of acceptance: [-∞: 6.9443].

.So, it's not statistically significant.

In **Lymphocyte count** Among intervention since p-value > α, H0 cannot be rejected.

The p-value equals 0.1207, (p(x≤3.7559) = 0.8793). The test statistic FA equals 3.7559, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group since p-value > α, H0 cannot be rejected. The p-value equals 0.3511, (p(x≤1.3755) = 0.6489). The test statistic FA equals 1.3755, which is in the 95% region of acceptance: [-∞: 6.9443].So, it's not statistically significant

In **Eosinophil Count** Among intervention Since p-value > α, H0 cannot be rejected. The p-value equals 0.1098, (p(x≤4.0347) = 0.8902). The test statistic

FA equals 4.0347, which is in the 95% region of acceptance: [-∞: 6.9443]. Among group Since p-value > α, H0 cannot be rejected.

The p-value equals 0.1098, ($p(x \leq 4.0347) = 0.8902$). The test statistic FA equals 4.0347, which is in the 95% region of acceptance: [-∞: 6.9443].So, it's not statistically significant

6. DISCUSSION

Fever is the abnormal elevation of temperature above 37.2^0C in the evening. The temperature is elevated by increasing heat production and reducing heat loss(1). Fever is the most common presenting symptom of a varied group of disease. Fever is a complex pathological process that manifests itself as a regulated elevation of body temperature over the normal circadian variations. The living organisms are classified into two groups depending upon the maintenance of body temperature namely homeothermic and poikilothermic animals(36). Now a days fever is the most panic symptom in the world because of COVID 19. In this time we can show the power of homoeopathy with symptomatic treatment. Arsenicum album is widely used medicine for covid 19 symptoms. in this study also done with Arsenicum album.

From the study it was found that arsenicum album ranks highest in reducing body temperature compare with paracetamol. This indicates that Arsenicum Album 200 helps to maintaining the body temperature occurs from any cause. In this study we checkout the blood

parameters which were increased during infections. there also we can understood that homoeopathic medicine Arsenicum Album has the power to change the level of blood parameters that means it comes to normal after giving Arsenicum Album 200. but in case of paracetamol changes in blood parameters doesn't come normal even after body temperature become normal. from this we can understand that homoeopathic medicine cure a disease from its root but paracetamol cures symptoms only infection persist inside the body.

The study was done in cape bio research lab at Marthandam. Before starting the study the albino rats were divided into three groups and each have 6 numbers of rats. Animals will be caged with a maximum of 2 animals each in a polypropylene cage and fed with standard food pellets and water. Three groups of rats will be treated with 135mg/kg baker's yeast (saccharomyces cerevisiae) suspended in 10 ml of normal saline will be induced intraperitoneal for fever induction. Before injecting baker's yeast moniter the temperature of every rat and Temperature will be monitored 4 hours after induction of bakers yeast.Group1 receives serves as control group. Group 2 treated with paracetamol 1mg/kg4 hourly by oral feeding needle. Group 3- orally treated with arsenicum album 200 five drops four hourly by oral feeding needle. Temperaure was monitor every hourly after the administration of drug. intervention was made at the intervals of 4^{th} hour. In this study we consider total blood count, neutrophil, eosinophil, lymphocyte and platelet count were checked along with temperature monitoring.

Group 1 that is control group animals show sudden raise of temperature and gradually decreases. but doesn't show any improvement.. group 2 animals shows sudden decreasing of temperature after giving paracetamol. that suddenly increase when the medicinal acti on is end. then group 3 shows sudden increase of temperature for some hours and then decreases gradually and comes to normal range after administering medicine. When comparing the blood parameters after Baker's Yeast induction and after intervention it is seen that Total blood count got slightly increased in all the three groups and Platelets and Neutrophil count remained at the same level after intervention. In Group 1 treated with Normal Saline the lymphocyte count remained unchanged as before, while in Group 2 which was treated with Paracetamol showed a slight decrease in lymphocyte count and in Group 3 treated with Arsenicum album200 showed an increase in lymphocyte count. The Eosinophil count was decreased in all three group. The rats treated with Arsenicum Album 200 showed good immunogenic response compared to rats treated with Normal saline and Paracetamol.

This study shows the homoeopathic aggravation of medicine. that means after administering the remedy Arsenicum album 200 the pyrexia was increased fist then gradually decrease and comes to normal. it shows kents third observstion that is aggravation is quick, short and strong with rapid improvement of the patient. and also aphorism 157 to 161 in organon of medicine Hahneman explained

about the homoeopathic aggravation. In 158th aphorism it's given that "There will be slight Homoeopathic aggravation during the first hour. A very good prognostic that the acute disease will probably yield to the first dose is quite as it ought to be as the medicinal disease must naturally be, somewhat stronger than the malady to be cured if it is to overpower extinguish the latter. Just a natural disease can remove and annihilate another one similar to it only when it is stronger than the latter".

7. CONCLUSION

Arsenicum album is effective in controlling pyrexia in bakers yeast induced fever in wistar albino rat in 200 potency. It is more effective in reducing temperature when compare with control group and the group treated with paracetamol.

Study shows the Homoeopathic aggravation with rapid improvement in temperature in albino rat models. Homoeopathic medicine arsenic album shows better immunogenic response when compared with allopathic dose. The results were considered statistically significant at $p \leq 0.05$

The p-value is less than 0.05 for parameters such as temperature, total count, Platelet Count and For eosinophil , neutrophil and Lymphocyte count has p value is greater than 0.05 indicating that it is due to chance. If It is has got more time duration for the study it will become statistically significant.

8. SUMMARY

Fever was induced to a sample size 18 female wistar albino rats divided randomly into 3 groups containing 6 animals after 90 days of acclimatization. After inducing baker's yeast temperature will be monitored 4 hours. The blood sample will be drained from the rat tail once before the administration of drug and 24 hours 48 hours after the administration of drug.

It was found that among these group arsenicum album group showed highest result in decreasing pyrexia compared with paracetamol.

The test are significant with a p value <0.05, for all the parameters except for neutrophil, eosinophil, lymphocyte

6.1 LIMITATIONS

- Individualization not done in this study
- Limitation in selecting the potency
- Competence of homoeopaths to do an experimental study

- Acceptance by homoeopaths for an experimental study
- Challenging the concepts of disease which are dynamic in origin.
- Long duration is needed for understanding the changes in blood parameters. This would have help in understanding difference in variable among groups.

6.2 RECOMMENDATIONS

- Studies using animals models of different pathology and different medicines can be done
- The same study can be done using different medicine

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