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In-Vivo Method for Clinical Analysis of Polycythemia

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Abstract

Polycythemia is normally defined as blood disorder which causes an increase in hemoglobin or venous hematocrit above 65%. It occurs either in neonates or in people above 60 years. The hyper viscosity in new born at the age of two hours leads to cardiac arrest because of oxygen impairment. The clinical features of hyper viscosity affects all the organs in the body and this entity should be screened in high risk adults (above 60 yrs) and neonates. The causes for polycythemia may be genetic or physiological and the treatment varies accordingly. This technique, the selective removal of RBCs can provide sometime until the decision about the disease (genetic or physiological) and treatment is made by the physician. This can reduce the risk associated with the conventional methods followed so far and the risk of cardiac arrest in neonates and adults is reduced.

Keywords: Bio-microfilter, Hematocrit, Hyperviscosity, In-vivo, Polycythemia

1. Introduction

Polycythemia is a Greek word which means "too much of blood cells". Even though polycythemia produces an increase in all blood cells (RBCs, WBCs, Platelets), it classically increases the production of RBCs[1]. Polycythemia is a condition in which there is an increase in the percentage of blood volume that is occupied by red blood cells, which is measured as haematocrit level. When the level of hematocrit is greater than 52% in men and 48% in women[2] or when the hemoglobin level is greater than 18.5 g/dL in men. And 16.5g/dL in women, the condition is termed as Polycythemia. Due to hyper viscosity of blood, there is an oxygen impairment of tissue and high perfusion that leads to the formation of micro thrombi. The reduced blood flow due to hyper viscosity can lead to difficulties such as coagulation of blood, nose bleeding and gout. The hyper viscosity reduces the deformability of RBCs. The association of viscosity and haematocrit of blood is almost linear up to a 65% and then increases exponentially[3]. The emergency treatment of polycythemia is done by phlebotomy or venesection, the blood removed from the circulation is centrifuged from which the RBCs are removed and the remaining blood components are injected back to the patient. It is done regularly for few months in order to reduce the viscosity and until the RBC count becomes normal in blood[10].

There are two forms of polycythemia they are relative or absolute (true) polycythemia according to the blood volume and RBC stack. Relative polycythemia is an evident rise of the RBC level in the blood, although the main cause is to reduce the blood plasma. The causes of relative polycythemia is loss of body fluids, such as dehydration, through burns and stress[4,5]. Absolute polycythemia is an excess production of RBCs which is due to myeloproliferative syndrome (a primary process in the bone marrow) or it may be a response to inveterate low oxygen levels or malignancy (rarely). Absolute polycythemia can be divided into two types. They are primary polycythemia and secondary polycythemia. The causes for primary polycythemia is due to an inherent problems in the process of red blood cell production. Primary polycythemia mutations causes abnormally high levels of red blood cell precursors which is due to acquired or inherited genetic. Primary Familial and Congenital Polycythemia (PFCP) and Polycythemia Vera (PV) Secondary polycythemia is due to an increase in red blood cell production to compensate for oxygen deficiency (hypoxia)[7]. This has been observed in patients with chronic pulmonary disease, congenital heart disease and renal disease, chronic lung disease, cigarette or cigar

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smoking. Secondary polycythemia can also cause due to some tumours, particularly brain, renal disease, and lung carcinomas that produce a substance like red blood cells[6]. Polycythemia can be both symptomatic and asymptomatic. Asymptomatic polycythemia is known as none identified symptoms or presenting no symptoms of disease[8,9].

The conventional methods for polycythemia followed so far is Exchange Transfusion method (Ex-Tx). In general exchange transfusion in blood is to transfer blood from one patient to another or to put red blood cells in the patient's body due to various blood disorders. Exchange Transfusion in Polycythemia is done by placing a needle into median vein and allowing some of the patient's blood to drain through a plastic tube into a bottle[11]. This reduces the amount of blood cells and makes the patient to feel better. The amount of blood drained is different for everyone according to the patient's size and severity of illness. In general 5 to 20 mL of blood is removed from the patient each time. The blood taken out is centrifuged in which the RBCs, WBCs and plasma are separated. The WBCs and plasma are injected back to the patient which means some of the red blood cells are removed through centrifugation. The process is repeated until the RBC count becomes normal. This application is good for adult patients but not neonatal because of their relatively immature immune system, transmitted diseases due to transfusion in infants can cause serious consequences[12].

The risk factors of exchange transfusion method are blood clots, changes in blood chemistry such as high or low potassium, low calcium, low glucose, heart and lung problems due to insufficient blood transfusion, changes in acid base balance, infection due to unclean syringe needles, bacterial contamination in blood[13,14].

The other conventional method used is Rehydration for pregnant women. Amniotic fluid is the major part of a pregnant women which acts as a protective bag or cousin for the fetus against the pressure and stress placed on the abdomen. The mother's blood volume plays a vital role in maintaining the amniotic fluid volume for carrying the fetus. The hydration status and maternal plasma osmolality can also alter amniotic fluid volume with prevents the neonatal mortality[15]. This rehydration technique is done for pregnant women whose body gets dehydrated with insufficient of fluid intake which may affect the fetus with polycythemia. If a pregnant woman is affected by serious dehydration, the mother should be treated with IV fluid injection or oral rehydration therapy for every two hours under physician observation.

The risk factors of rehydration for pregnant women is due to excess of rehydration or over-hydration bursting of amniotic fluid which causes early pregnancy, proper amount of fluid must be intravenously delivered[16].

2. Materials and Methods Used

The selective removal RBC for polycythemia using in-vivo method can be done by determining the various diameter range of blood components. Initially the amount of blood to be sucked out from the patient must be calculated according to the patient's size and severity. A needle is used to puncture the patient's vein to draw the blood out of the body. Since the diameter range of RBC is very small when compared to the diameter range of WBC, a micro filter (ranges in the size of RBC) is used for sucking up or removing only RBCs from the blood through the needle, while the WBC and plasma flows through the blood vessel normally.

3. Experimental Setup

A microcontroller or a computer is used for operating the suction motor which has a pre-set value for sucking the amount of RBCs from the blood. It also gives a feedback to the physician about the fluid loss compensation. If there is any fluid loss (plasma fluid) the patient can be treated with IV plasma fluid under physician's observation[17].

The diameter range of various blood components such as Red Blood Cells and White Blood Cells are studied. The diameter range of RBC is approximately 6.2 to 8.2 μm and a thickness at the thickest point of 2 to 2.5 μm and a minimum thickness in the centre of 0.8 to 1 μm. Red Blood Cell is the much smaller than most other human cells. The life span of RBC is 120 days and they are mainly respon-

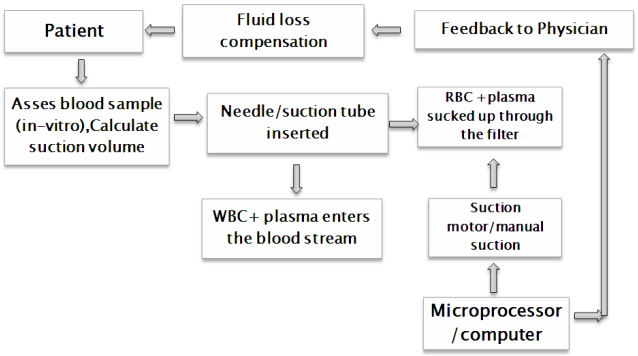

Figure 1.

sible for oxygen transportation. The diameter range of WBC is approximately greater than 10 µm. There are five types of white blood cells (leukocyte). These are divided into two main classes Granulocytes (includes Neutrophils, Eosinophils and Basophils) Agranulocytes (includes Lymphocytes and Monocytes). Lymphocytes vary widely in size. Small lymphocytes are 7 to 10 µm in diameter, and large lymphocytes are approximately 14 to 20 µm in diameter. Monocytes are approximately 15 to 25 µm in diameter[18]. Neutrophils constitute 60 to 70 per cent of circulating white blood cells. They are 12 to 15 µm in diameter. Eosinophils constitute 2 to 4 per cent of circulating white blood cells. The cell is 12 to 15 µm in diameter and usually has a bilobed nucleus. Basophils are less than 1 per cent of the circulating WBCs and they are 12 to 15 µm in diameter.

The automatic syringe suction is done with the help of a robotic model which is controlled by 4 DC motors and an 8051 microcontroller. In general a microcontroller consists the circuitry of microprocessor as well as an in built ROM, RAM, I/O device, timer and counters, in-built memory and input/output devices takes less access time and for data and code it has separate memory map.

The 8051 is an 8-bit microcontroller which is intended by Intel. The 8051 microcontroller is constructed in N-Channel Metal Oxide Silicon (NMOS) and Complementary Metal Oxide Silicon (CMOS). It has the following advantages such as efficient and adaptable interrupt system, low-power operation, bit addressable space for minimum interrupt prolog/epilog, fast input and output operations and fast access to on chip RAM in data space. In this technique the 8051 microcontroller is programmed for the movement of the DC motor. The program is written in Keil µ VISION. The Keil development Tools are deliberated for professional software developer that helps the embedded microcontroller architectures. For 8051 microcontroller Keil µ Vision software supports C language directly. The 40 pin 8051 microcontroller chip is placed in the programmer kit and the program used is fed to the IC for various applications.

A microcontroller (8051) is used for pre-setting the values, for the amount of blood to be drawn out of the patient. This pre-set value is calculated according to the severity of illness, size and age of the patient. Minimum amount of blood is drawn out in neonatal since the new born's volume is too small. In adult patients (above 60yrs) the blood to be drawn out is calculated according to severity of polycythemia or excess RBC production in the blood. Relay is an electrically operated switch or electromagnetic switch. It is used in every type of electronic device when it is necessary to control a circuit by a low-power signal or where several circuit must be controlled by a switch. The electronic pulses perform switching in relay which do not require human interaction.

4. Program for Robotic Model

```
#include <AT89X52.H>
sbit Rs = 0xA7;
sbit Rw = 0xA6;
sbit En = 0xA5;
sbit inp = 0x90;
sfr P22 = 0xB0;
void init(void);
void write(unsigned int initial_value);
void line_1(int position_1);
void line_2(int position_2);
void write_char(unsigned char character);
void write_str(unsigned char *string);
void delay(long small_integer);
void display_ADC(unsigned int dec_output,int line_
num, int line_pos);
unsigned int j = 0,i,limit,div,adc_array[4];
void main(void)
{
  init();
  line_1(0);
  write_str("car movement");
  line_2(0);
  write_str(" DISTANCE=5cm ");
  inp = 0;
  while(1)
  {
   if(inp == 1)
    {
     while(inp == 1)
     {
       display_ADC(j++,2,7);
       delay(15000);
     }
    }
     else
     {
       while(inp == 0)
       {
  if(j != 0)
      display_ADC(j--,2,7);
  delay(15000);
       }
```

```
        }
     }
}
void display_ADC(unsigned int dec_output,int line_
num, int line_pos)
{
 if(line_num == 1)
   line_1(line_pos);
 else if(line_num == 2)
   line_2(line_pos);
 write_str(" ");
   if(line_num == 1)
 line_1(line_pos);
   else if(line_num == 2)
 line_2(line_pos);
 if(dec_output<=9)
 {
 limit = 1;div = 1;
 }
 else if((dec_output>9) && (dec_output<=99))
 {
   limit = 2;div = 10;
 }
 else if((dec_output>99)&&(dec_output<=999))
 {
   limit = 3;div = 100;
 }
 else if((dec_output>999)&&(dec_output<=9999))
 {
   limit = 4;div = 1000;
 }
 i = 0;
while(i < limit)
 {
     adc_array[i] = dec_output/div;
     dec_output %= div;
     div /= 10;
     write_char(adc_array[i++]+48);
   }
}
void init(void)
{
 delay(10000);
 write(0x38);
 write(0x06);
 write(0x0C);
 write(0x01);
 }
void write(unsigned int initial_value)
{
 P22 = initial_value;
 Rs = 0;       // 0 for ADDRESS
 Rw = 0;       // 0 for WRITE OPERATION
 En = 1;       // 1 -> 0 for WRITE OPERATION
 delay(100);
 En = 0;
}
//Selecting POSITION in LCD
void line_1(int position_1)
{
    write(0x80 + position_1);
}
   void line_2(int position_2)
{
    write(0xC0 + position_2);
}
//Writing DATA in LCD
void write_char(unsigned char character)
{
 P22 = character;
 Rs = 1;         // 1 for DATA
 Rw = 0;         // 0 for WRITE OPERATION
 En = 1;         // 1 -> 0 for WRITE OPERATION
 delay(100);   // need to be 100
 En = 0;
}
void write_str(unsigned char *string)// ABU
{
    while(*string)//->ABU >BU >U
 {
 P22 = *string++; //->ABU >BU >U
 Rs = 1;         // 1 for DATA
 Rw = 0;         // 0 for WRITE OPERATION
 En = 1;          // 1 -> 0 for WRITE OPERATION
 delay(100);
 En = 0;
 }
}
//Delay FUNCTION
void delay(long small_integer)
{
    while(small_integer > 0)
  {
    small_integer--;
  }
}
```

5. Mechanical Setup

The amount to blood to be sucked out is calculated according to the size and severity of illness in the polycythemia patient. The needle of the syringe is inserted in the median vein for drawing out the blood. A 8 μm filter is used for selective removal of RBC from blood because the diameter range of Red Blood Cell is approximately 6.2 to 8.2 μm. The micro filter is attached in between the syringe and needle which filters only the RBCs from the blood and allows the WBCs and plasma to flow along the blood stream normally. The filter used for the selective removal of red cells from the blood is disposable.

6. Result

The blood is removed from the median cubital vein and filtered through the 8 μm filter attached to the venflon and the robotic model for automatic syringe suction. The blood drawn out through the filter contains only RBCs and remaining blood components enters the blood circulation.

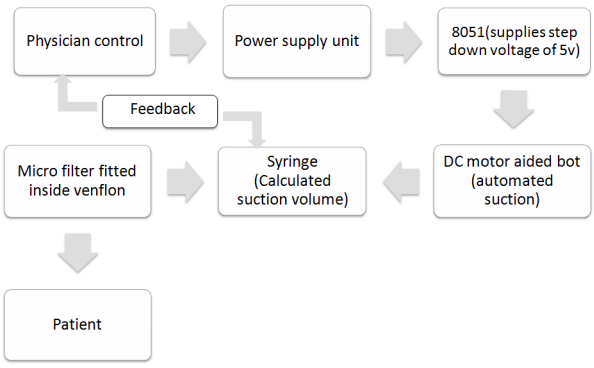

Figure 2.

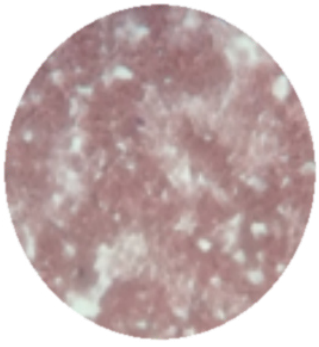

Figure 3. Presence of RBC with the absence of WBC under microscope (40x magnification) when tested with the micro-filter.

7. Conclusion

Polycythemia being one of the complicated physiological conditions in neonatal we conclude with the assurance that this instrument designed will definitely assist in reducing the mortality in new born. It also helps in reducing the risk produced by various traditional methods. This instrument can also be developed further to provide complete solution to polycythemia patients. This selective removal of RBCs can be developed by excluding plasma in future. This method can be developed and a complete reduction in exchange transfusion method (traditional method) can be performed. A complete cure for polycythemia can be achieved. This method can help in extending research for neonatal polycythemia.

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