Stem Cell Therapy for Type 1 Diabetes

Dr. Sagar Arvind Jawale

Pediatric and neonatal surgeon and pediatric urologist

Email: drsagarjawale@gmail.com

Mobile No: 9370000380

Jawale hospital, Near SBI, Jilha Peth, Gandhi Nagar, Jalgaon-425001

Jawale Institute of Pediatric Surgery

Introduction: What are Stem Cells?

Adult stem cells are of 2 types, mesenchymal and haemopoietic stem cells which have potential to duplicate indefinitely and differentiate into 22 types of cells. The doubling time is only 3 days. These cells typically divide for up to 6 months making them into billions of cells. These cells produce 50 types of growth factors and cytokines which repair and differentiate adult tissues in an epigenetic manner. Stem cells put in a particular organ gets differentiated into cells of that organ due to particular growth factors produced by that particular tissue. Mesenchymal stem cells have the ability to differentiate into tissues of all 3 lineages a phenomenon called plasticity.

Introduction continued

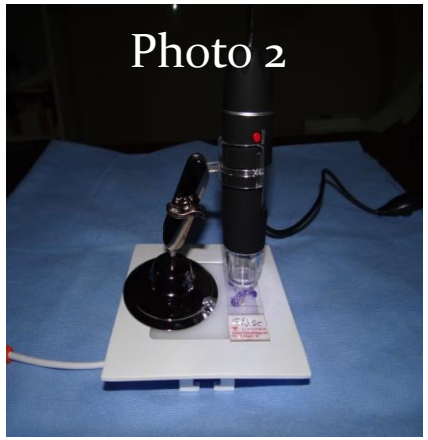
Whenever a particular organ undergoes damage, stem cells in that area come fore-wards and get differentiated into specialized cells and the damage is replenished. But when the damage is extensive, the organ starts failing. By doing stem cell therapy we harvest stem cells from other healthy tissues as fat and bone marrow and put them into the diseased organ and these cells now get differentiated into specialized cells and the organ starts functioning again. In health stem cells from fat or bone marrow can not migrate into diseased organs, hence it is necessary to transplant them.

Guidelines For Stem Cell Research

Institutional Ethics Committee (IEC) permission taken and institutional Committee for Stem Cell Research(IC-SCR) established at city level for peer review of stem cell research. Two visiting stem cell experts attached to the center with M. Phil degree in regenerative medicine. Collaboration done with Thermo Fischer Scientific, the world's largest cell media company. Money raised from Rotary club, Lion's club, MLA fund and other NGOs and patient's were not charged for the study. In short my stem cell research in in tune with the government of India's guidelines.

Stem Cell Laboratory

Stem cell laboratory needs a centrifuge machine(Photo1), reagents(Photo3) for separation of stem cells by density gradient method, a microscope(Photo2) and photo activation device(Photo4) for photo stimulation of stem cells and incubator. It was Set in just USD 500 instead of USD 50,000 in the market. The cost of autologous stem cell transplantation dropped to USD 1000 in my hospital compared to USD 5000 in India.



Stem Cell Therapy For Type 1 Diabetes

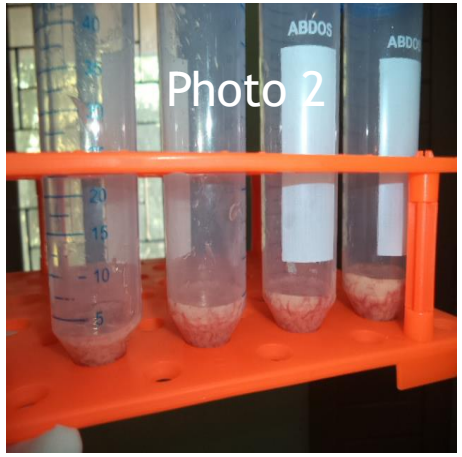
Introduction: Type 1 diabetes is a dreadful autoimmune disease of childhood with incidence of 0.26/1000 children in India. Currently insulin injection and islet cell transplantation are the FDA approved treatments. Taking multiple insulin shots daily and its cost are both unacceptable to most of the children. Islet cell transplantation is exorbitantly costly and gives relief only for 2-5 years. Hence a new, cheap and effective method needs to be developed for the treatment of this disease. I invented an "Omental Pouch Stem Cell Operation" for children below 10 years and "Intra-pancreatic Stem Cell Implantation" operation for Type 1 diabetes patients above 10-year age. Both the operations are reported for the first time in the medical literature.

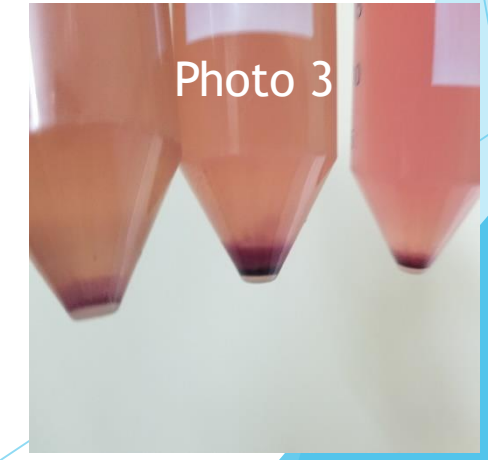
Materials and Methods

Last 3 years I treated 21 patients of Type 1 diabetes with Omental Pouch Stem Cell Operation where autologous bone marrow derived stem cells were put into an Omental pouch and peritoneum. Age range was 6 month to 10 years. All patients were Insulin dependent diabetes. Blood sugar F/PP, Anti Gad antibody titer, Glycosylated Hb and C peptide levels were done before the therapy and thereafter at every 3 monthly intervals. Only 3 patients (14.28%) had auto immunity with significantly raised Anti Gad antibody levels.

Omental Fat Derived Stem Cells Surgical Technique

Since these children are malnourished small umbilical incision taken and half the omentum(Photo1) was excised to be used as a source for stem cells. It is reported for the first time in medical literature. The fat was finely chopped and put into 4 test tubes(Photo2) and stem cells obtained by enzymatic digestion of fat with Type 1 collagenase enzyme.(Photo3).The whole process involves 50 steps. After 12-16 hours, stem cells are ready.





Bone marrow derived stem cells

100-150 ml marrow was aspirated using a 50 ml syringe with heparin sodium as anticoagulants in a 10% solution. The collected bone marrow e.g. 25 ml is diluted with equal quantity of Dulbecco's Phosphate Buffered Saline with 2% Fetal Bovine Serum (PBS + 2% FBS). The diluted bone marrow is poured over equal quantity of density gradient such as Lymph prep or Histopaque with density of 1.077 g/mL into disposable centrifuge tubes of 50 ml capacity. The tubes are centrifuged at 800 ×g for 20 minutes at room temperature (15˚C - 25˚C) with brake of.

The Omental Pouch Stem Cell Operation

An Omental pouch was created and no 7 IFT put into it and another into the peritoneal cavity. This operation is reported for the first time in the medical literature. Fat processed by enzymatic digestion by collagenase type 1 enzyme and after 50 steps and 12-16 hours later stem cells are ready. One third quantity of stem cells are put into the Omental pouch, another one third into peritoneal cavity and another third given IV in 100 ml NS with 20 mg/kg methylprednisolone infusion over 1 hour.

Results

It took 3 months to see results. The sugar levels are regularly monitored and dose of insulin adjusted accordingly. At the end of one year, 7 (33.33%) patients went off insulin and are free of insulin till three year after therapy. Remaining 14 (66.67%) patients insulin requirements dropped to 50 % and sugar levels dropped from 50-75 % into the normal range. Anti GAD antibody titer dropped to about 50-75 % in 6 month indicating reversal of auto immunity. C peptide levels increased 50 % than before indicating increased endogenous insulin production. In the control group no patient was off insulin. 12 patients insulin requirement increased and 9 patients it was same in 3 year follow up. Anti GAD antibody titer, Glycosylated Hb levels and C peptide levels were almost same in control group.

Discussion

Scientists grew human stem cells in hyperglycemic environment in petri dishes and at the end of 3 months these cells transformed into pancreatic islet like cells and started producing insulin a phenomenon called plasticity. Stem cells were put into the peritoneal cavity of diabetic animals and these cells produced insulin at the end of 3 months. Stem cells given IV in diabetic animals repaired the damaged islet cells and also regenerated the islets of Langerhans. Stem cells given IV repaired the faulty signatures in T cells in an epigenetic manner and reversed autoimmunity. Above experiments are the foundation of stem cell therapy for Type 1 diabetes in humans. Peritoneal cavity has only 10% cellular immunity and omentum has negligible immunity on its surface. Stem cells put into an Omental pouch creates a new biological pancreas which is protected from auto immunity. The cost of operation was only USD 1000.

Conclusion

The Omental Stem Cell Pouch operation was cheap, safe and effective for Type 1 diabetes patients below 10 years. It also reversed auto immunity partially. Best results were obtained in children without auto immunity. Patients with auto immunity had relatively poor results.

Intrapancreatic Stem Cell Transplantation

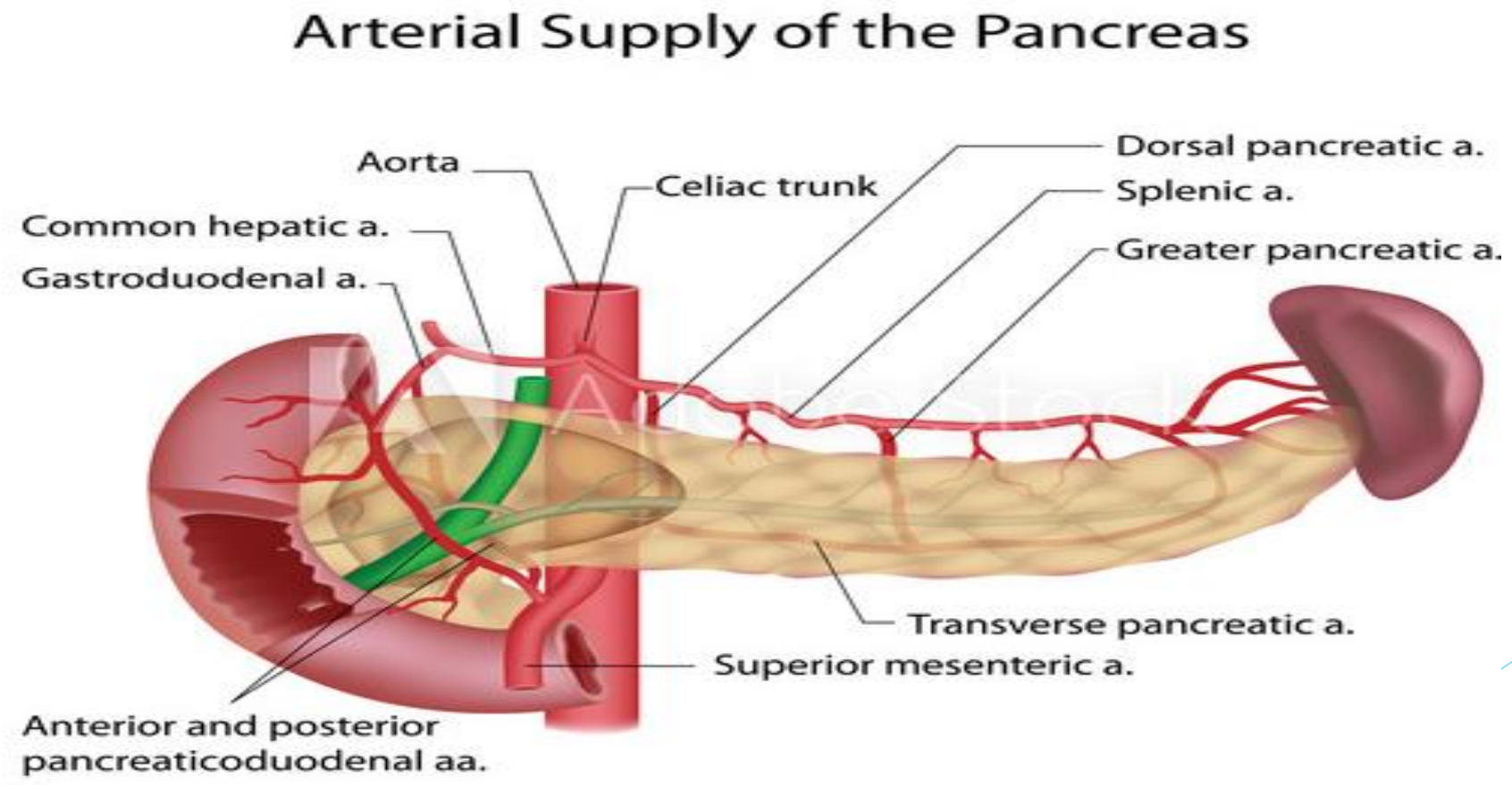
Introduction: Generally, stem cells are only put into the blood. Since pancreas gets only 2% of blood volume, it gets only 2 % of cells put into the blood. The results of stem cell therapy are directly proportional to the amount of stem cells infused. Hence, with interventional radiology, the pancreatic artery was cannulated in a Catheterization lab and stem cells were infused directly into pancreas. With this method the pancreas gets 90-95 % stem cells.

Materials and Methods

In my institute, in past 3 years I did 23 cases of Intra-pancreatic stem cell transplantation. The age range was 10 year to 56 year. All patients were Insulin dependent diabetes. In the same period, 26 patients of Type 1 diabetes were put as a control. Blood sugar F/PP, Anti Gad antibody titer, Glycosylated Hb and C peptide levels were done before the therapy and thereafter at every 3 monthly intervals. Only 5 patients (21.73%) had auto immunity with significantly raised Anti Gad antibody levels.

Blood Supply of Pancreas

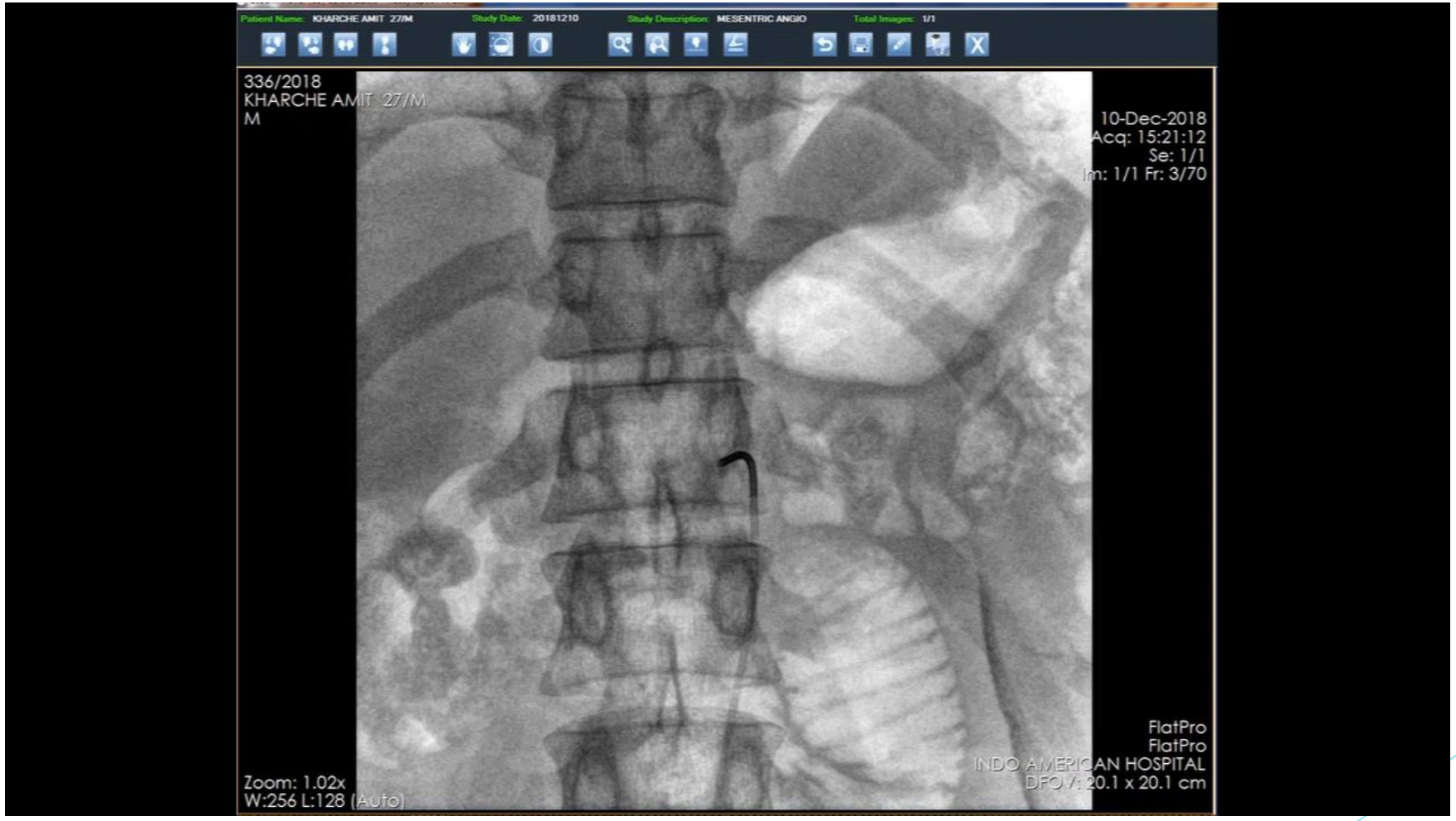
Pancreas is supplied by branches of gastro-duodenal and splenic artery. Branches of splenic artery, which extend to the body and to the tail of the gland include: dorsal pancreatic artery, inferior pancreatic artery, greater pancreatic artery, artery to tail of pancreas, and pancreatic branches.



Interventional radiology Technique

The patient is taken to a catheterization lab and through the femoral artery the pancreatic Artery is cannulated. 50 % cells are infused in Main pancreatic artery and another 50% cells in the Distal part of splenic artery as it supplies tail of The pancreas which has about 80 % Islets of Langerhans.

Pancreatic Angiogram



Results

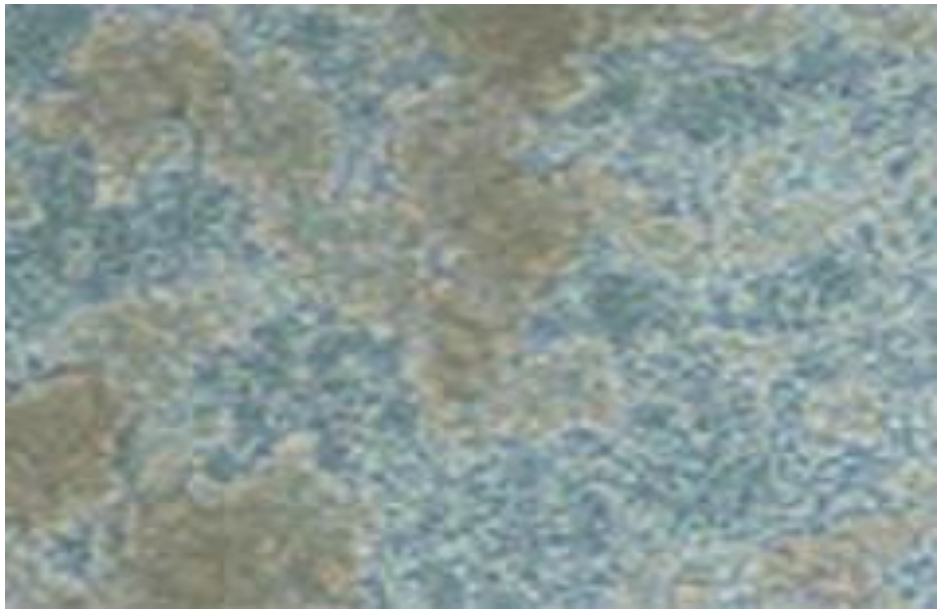
In intra-pancreatic group, 15 (65.21%) patients went off Insulin at the end of one year. Remaining 8 (34.8%) patient's insulin requirements dropped to 50 % and sugar levels dropped from 50-75 % into the normal range. Anti GAD antibody titer dropped to about 50-75 % in 6 month indicating reversal of auto immunity. C peptide levels increased 50 % than before indicating increased endogenous insulin production. In the control group no patient was off insulin. 15 patients insulin requirement increased and 11 patients it was same in 3 year follow up. Anti GAD antibody titer, Glycosylated Hb levels and C peptide levels were almost same in control group.

Discussion

Generally, stem cells are only put into the blood. Since pancreas gets only 2% of blood volume, it gets only 2 % of cells put into the blood. The results of stem cell therapy are directly proportional to the amount of stem cells infused. Hence, with interventional radiology, the pancreatic artery was cannulated in a Catheterization lab and stem cells were infused directly into pancreas. With this method the pancreas gets 90-95 % stem cells. Such a therapy is 30-50 times more powerful than putting cells into blood. The stem cells are a common raw material. The pancreatic tissue produces specific growth factors and cytokines which make the stem cells differentiate into Beta cells of the Islets of Langerhans. The 50 types of growth factors and cytokines releases by stem cells also repair and regenerate old Beta cells in Islets of Langerhans. According to 2 publications, the blood sugar levels drop steadily up to 2 years after single implantation. Total treatment cost was just USD 1500 instead of USD 50,000 in USA.

Future Prospects

Stem cells were cultured and transdifferentiated into islets of Langerhans at a negligible cost of USD 500 per billion islets in my laboratory compared to USD one million in USA. Photographs were taken and the cells discarded as implanting them to human body requires DCGI permission. I plan to produce Islets of Langerhans in laboratory and implant them into the Omental pouch to protect them from autoimmunity creating a biological pancreas. Alternatively, I also plan to inject stem cells into the pancreatic artery or the hepatic artery which is 50 times more powerful that IV option.



Conclusions

Stem cell therapy for Type 1 diabetes was affordable, safe, effective. My center developed world's first as well as the world's cheapest stem cell therapy costing only USD 1500 instead of USD 50,000 in USA. Below 10 years of age, the Omental Stem Cell Pouch operation was preferred. Above 10 years of age, the intra-pancreatic stem cell implantation was preferred. Early results of stem cell therapy for Type 1 diabetes are encouraging, although we need far bigger number of patients and a longer follow up.

Since my stem cell therapy and research is made possible at a district place and not in a tertiary health care center, it means than many doctors in India can do it even in Taluka places, hence it creates a lot of hope for millions of people in India and worldwide.

Thank You

Dr Sagar Arvind Jawale

Pediatric and neonatal surgeon and pediatric urologist

Email: drsagarjawale@gmail.com

Mobile No: 9370000380

Jawale hospital, Near SBI, Jilha Peth, Gandhi Nagar, Jalgaon-425001