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Editorial

Corneal Transplant; Changing Trends of The Twenty First Century and Where Do We Stand?

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According to the World Health Organization, corneal blindness accounts for the 4th leading cause of global blindness after cataract, glaucoma and age-related macular degeneration.[1] Major causes of corneal blindness include Keratoconus, infectious keratitis, Vitamin A deficiency, inherited corneal diseases, corneal degenerations, corneal dystrophies and trauma. In a country like Pakistan, poor rural communities are prone to increased risk of contaminated corneal injuries and infectious corneal diseases while the health facilities are scarce leading to an increased frequency of cornea associated visual impairment.

To tackle corneal blindness, Penetrating Keratoplasty (PK) was introduced in 1905 by Eduard Zirms.[3] Itremained the only corneal transplant option for a long time till the middle of twentieth century. With technological evolution in every field of science, new surgical techniques in Keratoplasty were also developed. As the understanding of the corneal anatomy and physiology further improved, the idea of partial thickness corneal grafts became a special consideration of the corneal surgeons. This was followed by superficial and deep anterior lamellar Keratoplasties, in cases where corneal endothelium was healthy.

Burden of the corneal disease was further increased with the iatrogenic corneal insult caused by surgical trauma during cataract surgery. With the advent of phacoemulsification, which has a long learning curve, there was an increase in the number of patients with pseudophakic bullous keratopathy. According to one study, even in uncomplicated phacoemulsification there was 9% endothelial cell loss during one year after surgery.[2] Although, it does not have detrimental effectson a healthy cornea but in eyes with already compromised corneal endothelium, this can lead to disaster. The rate of corneal endothelial cell loss is definitely high if the surgery is performed by a beginner.

A healthy corneal endothelium is vital for corneal transparency. In a new born, corneal endothelium consists of around 6000 cells/mm,[2] which falls with the advancing age at a rate of 0.6% each year. Any trauma to the endothelium, which results in excessive corneal endothelial cell loss, will lead to corneal edema and loss of corneal transparency. Thus the focus started to change from full thickness corneal grafts to partial thickness posterior lamellar Keratoplasty. A time came when corneal endothelium transplant was thought to be a more useful procedure to tackle endothelial dysfunction. In 1998, posterior lamellar Keratoplasty was performed in animals and cadaver eyes by Gerrit.[4] It was followed by Descemet stripping endothelial Keratoplasty (DSEK). In 2006, microkeratome was introduced in this field and grafts were prepared using microkeratome leading to procedure called Descemet stripping automated endothelial Keratoplasty (DSAEK).[5] This was indeed a game changer in the field of corneal transplant. It is a

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minimally invasive procedure avoiding open sky technique of PK. Endothelial transplant procedures proved to have better tensile strength of cornea as compared to the full thickness corneal transplant procedures. Further improvement was brought about by a more improved and thin corneal graft. It was observed that decreasing the graft thickness to less than 100 microns resulted in better visual outcomes. In ultrathin DSAEK, patients achieved visual acuity of 20/20.[6] This resulted in the development of a new technique called Descemet's membrane endothelial keratoplasty (DMEK). In this procedure, the graft thickness was reduced to approximately 10 μm.[6]

Advancement in today's Keratoplasty is the use of intra-operative OCT, which can be used to measure the central corneal thickness of the host and donor cornea. FALK or femto laser assisted lamellar Keratoplasty is another breakthrough for sharp and accurate cuts of the donor as well as host tissue, leading to perfection of the procedure and minimizing post-operative complications.

New developments always bring new challenges. Demand of corneal tissue increased with the successful transplant surgeries leading to an imbalance between the demand and supply of corneal tissue. Scientists began to think about the alternatives and this led to introduction of newer techniques. In 2017, Descemet stripping only (DSO) technique, also called Descemetorhexis without endothelial keratoplasty (DWEK) was introduced. In this technique, central 4mm zone of Descemet membrane was removed without transplant. This technique is useful for central endothelial disease with normal corneal periphery. Minimum endothelial count required for this procedure to be successful is more than 1000 cells per square millimeter.[7]This procedure was improved upon by the use of Rho kinase (ROCK) inhibitor which facilitates endothelial migration towards the corneal center. Recently, Ripasudil has shown good results in patients undergoing DSO.[8] This drug reduced the recovery time of the patient from an average of 6.5 weeks to 4.6 weeks.

Cell culture technology for corneal endothelium was another breakthrough in corneal transplant journey. In this technique, endothelial cells are obtained from a single donor, cultured and can be transplanted into many patients. Kinoshita and his colleagues conducted first human trial of cultivated corneal endothelial cells in cases with bullous keratopathy.[9] They injected cultured endothelial cells in the anterior chamber and injected Rho kinase inhibitors. After injection of air in the anterior chamber, the patient was asked to lie down in the face down position for three hours to help adhesion of the endothelial cells. A 5 – year follow up study of 11 patients has been published which has opened new horizons for the corneal disease management.[10] This procedure once established for human use will not only overcome the problem of donors but there will be an additional advantage of cultured endothelial cells to be stored for extended time period.Another advantage of cell culture is that the mesenchymal cells can be obtained from the patient him/herself, which decreases the chances of immunological reactions. This procedure can be repeated as well. There is still a long way to go in this field. Which mesenchymal cells have best results, how long they can be stored, what is the minimum number of cells needed for corneal endothelial layer recovery, what are the factors that can improve the efficacy of this technique, all these questions need to be answered?

Another quantum leap is the Bioengineered corneal transplant surgeries. This is done in cases where all the above mentioned maneuvers have failed. Bioengineered Keratoprosthesis is the last resort in refractory corneal diseases. Although few types of keratoprosthesis are available but their importance in multiple failed grafts and corneal autoimmune diseases cannot be overlooked.

In Pakistan we have to go a long way in this field. Much work needs to be done in the private and the public sector because of the huge burden of corneal blindness in our country. Like any other organ donation in Pakistan, there are cultural as well as religious issues along with the ethical considerations regarding corneal transplant. Another hurdle is the availability of corneas. Ninety percent of the corneas used in Pakistan are imported. We need to become self-sufficient but this requires public education. Religious scholars have to play a pivotal role and the role of the state comes into play in case of unclaimed dead bodies. To add further to the already existing challenges, health care system of Pakistan has remained unattended for long. Time has come to develop an up to date database in the health sector where all the record of the donor and host tissues should be maintained and retrieved when needed.

Conflict of Interest

Authors declared no conflict of interest.

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Author's Designation and Contribution

Tayyaba Gul Malik; Professor of Ophthalmology: *Concepts, Literature search, Manuscript preparation, Manuscript review.*