بسم الله الرحمن الرحيم

The study of relationship between serum levels of soluble VEGF receptor-1with delayed graft function after kidney transplantation

authors

Zahra Chitsazian

Hossein Akbari

Behzad Einollahi

Hassan Nikoueinejad

Zahra hooshyar

Saeede Shabanitabar

Introduction :

➤Human kidney transplantation is the most effective treatment of chronic advanced renal failure.

➤ Although this method relieves patients of many complications of dialysis, it has some complications on its own.

➤ One of which is Delayed Graft Function (DGF) accelerating 10% rate of rejection.

❖ Soluble fms-like tyrosine kinase-1 (sFlt-1) is a splice variant of VEGF receptor-1

❖ It also occupies VEGF receptors preventing its binding and path signaling. Thus, reducing the effectiveness of VEGF in the presence of increased levels of sFlt-1 seems likely .For example a study showed that the level of sFLT-1 is significantly higher in patients with PHT in SCD patients

❖ Such concept has not been addressed as a reason of DGF so far. Improved DGF in the presence of decreased levels of sFlt-1can indorse our theory. If so, using sFlt-1 blocker antibodies, we may be able to treat DGF, which in addition to faster return of kidney function after transplantation.

Materials and Methods :

• This case-control study was performed on 2 groups of 58 kidney transplantpatients with and without DGF. Each patient was followed for a period of 6 months.

• The control group was selected from the patients who underwent a transplant and did not show the mentioned DGF criteria at the end of the first week. DGF and control group patients were fallowed within 6 months on a monthly basis and were studied for the type of prescribed immunosuppressive drugs, CMV infection, infections leading to hospitalization, and acute rejection.

Measurements :

❑ A serum sample was prepared from all participants and kept at -20. Once collected, the samples were sent to laboratory and serum levels of sFlt-1 were evaluated by sandwich ELISA, eBioscienceUSA, according to kit recommendations.

❑ CMV infection was identified according to qualitativePCR,Primer design England kits on all participants.

Results :

✓ Serum sFlt-1 levels were significantly higher in DGF group compared to those in control group (P≤0.001).

✓ Respiratory, urinary, and CMV infection significantly increased the chance of DGF more than 10, 6.5, and 30 times, respectively (P≤0.001).DGF, Bk infection, respiratory, and urinary infection significantly increased the level of sFtl-1 by 2, 1.6, 1.4, and 3%, respectively (P≤0.017).

✓ Using logistic regression model, we showed that DGF is affected by sflt1 levels (p<0.001) .Such impact was found in the presence of taking cyclosporine and patients' age .

✓ The model illustrated that DGF risk increases by aging and increasing SFlt-1 (OR>1) and decreases with cyclosporine (OR<0.15). No other multivariate effects of other factors were observed. The model showed a high power of expression (R^2=0.676).

✓ Using ROC curve and Area Under Curve (AUC), we determined both sensitivity and specificity of diagnosis of DGF as 93.1% and 96.5%, respectively. Analysis of ROC in cut point of 64.7 has shown 91.4%sensitivity and 76% specificity (AUC=0.955)