EFFECTIVENESS AND SAFETY OF SOFOSBUVIR-BASED THERAPY OF CHRONIC HEPATITIS C IN PATIENTS AFTER KIDNEY TRANSPLANTATION

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Background

The introduction of direct acting antivirals (DAA) to the therapy of chronic hepatitis C made significant breakthrough in the effectiveness and safety and provided an access to such treatment of also kidney transplant recipients (KTR) who could not be treated with standard interferon based therapy. Till now, there are only a few published observations in this population.

The aim of the study was to assess the effectiveness and safety of new DAA therapy in stable KTR.

Material and methods

Out of 70 KTR with presence of anti-HCV antibodies, the HCV-RNA was detected in 35 patients. These patients were qualified to therapy. Clinical characteristics of the patients is presented in Table 1.

Table 1. Clinical characteristics of the patients	N=35
Sex	20M/15K
Age	49,6±6,4
Mean time after transplantation	10,4±7.3 lat
HCV genotype	
1b	26 (79%)
2a	2 (6%)
3	3 (9%)
4	2 (6%)
Viremia	2,81x10^6 IU/ml ± 4351,54
Fibrosis	
F0/FI/FII	28 (3/23/2) (71%)
FIII/FIV	7 (5/2) (29%)
ALT	46,51±85,56 U/l
AST	38,41±48,08 U/l
GGT	48,68±66,47 U/l
Creatinine	143,01±27,42 µmol/dl
eGFR	56.2±26,2 ml/min

GT1- and GT4-infected KTR were treated 12 weeks (first eight patients for 24 weeks) with 400 mg of sofosbuvir (SOF) and 90 mg of ledipasvir (LDV), with initial dose of ribavirin (RBV) 0-800 mg depending on the starting hemoglobin level. Patients infected with GT2 and GT3 were treated for 24 weeks with 400mg SOF with initial dose of RBV 200-800mg. The effectiveness of therapy was analyzed by assessing of rapid virologic response (RVR), end-therapeutic response (ETR) and sustained virologic response (SVR12) defined as an undetectable serum hepatitis C virus (HCV) RNA level at *week 4, the end of therapy and after 12 weeks after treatment, respectively.* Safety of therapy was monitored by repeated estimation of GFR (eGFR) and measurement of blood haemoglobin (Hb) concentration.

Results

The effectiveness of SOF-based therapy is presented in Fig.1. The RVR (n=33), ETR (n=26) and SVR12 (n=20) rates were 100%.

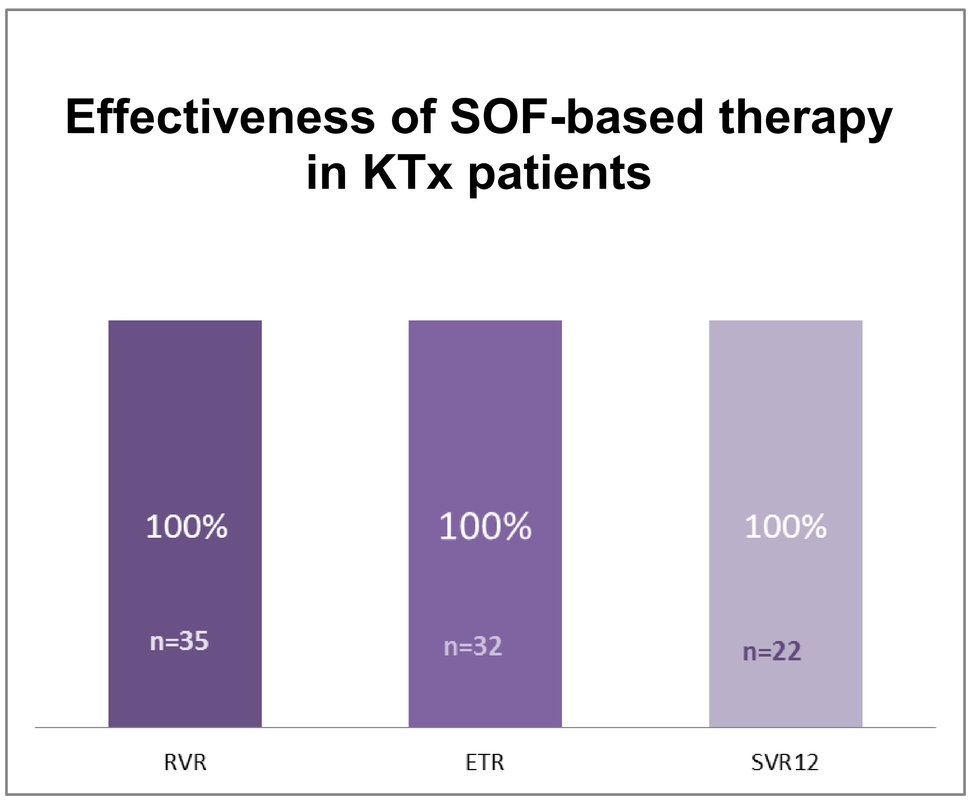

Fig. 1. RVR – rapid virologic response; ETR – end of treatment response; SVR12 – sustained virologic response

The therapy did not significantly influence eGFR (56.2±26,2 vs 53.9±25,7ml/min before DAA therapy, p=0,075) – Fig.2

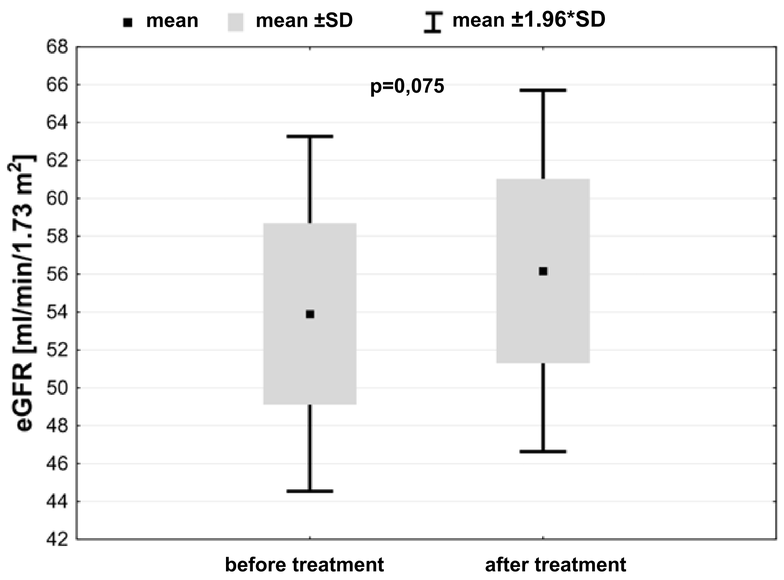

Fig. 2. The mean eGFR levels observed during antiviral treatment.

The mean initial blood Hb concentration was 13.59±1.93g/dl, range 9.2-19.1 g/dl, and after 4 weeks it decreased to 11.6±1.89 g/dl, range 8.1-16.2 g/dl (p<0.001) – Fig.3 and 4. RBV administration was modified according to product characteristics, leading to improvement of Hb level in most of patients. RBV had to be discontinued in 4 patients because of severe anaemia, and in one infected with GT3 with SOF/RBV-treated patient, the therapy was completely interrupted after 6 weeks. Two patients required single blood transfusion and erythropoietin supplementation. Disturbances of blood Hb concentration disappeared one month after the end of treatment.

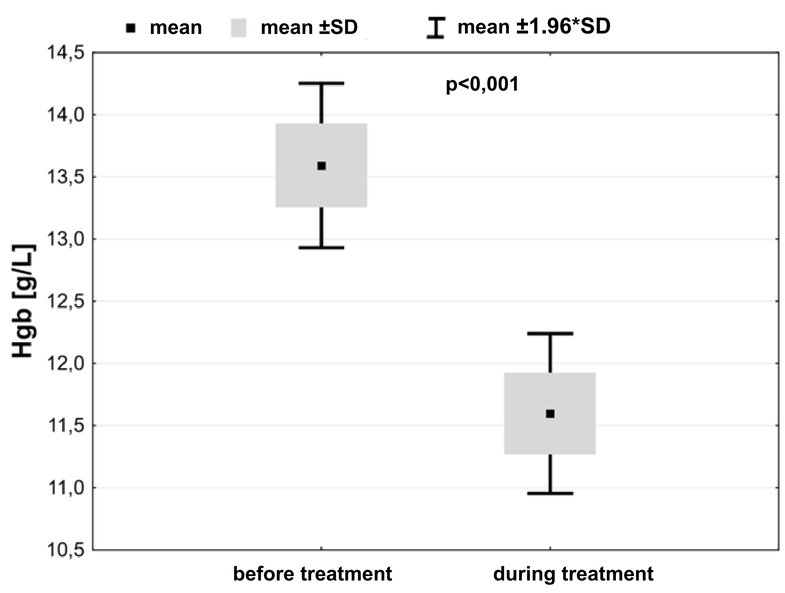

Fig. 3. Mean change in hemoglobin concentration observed after 4 weeks of antiviral therapy .

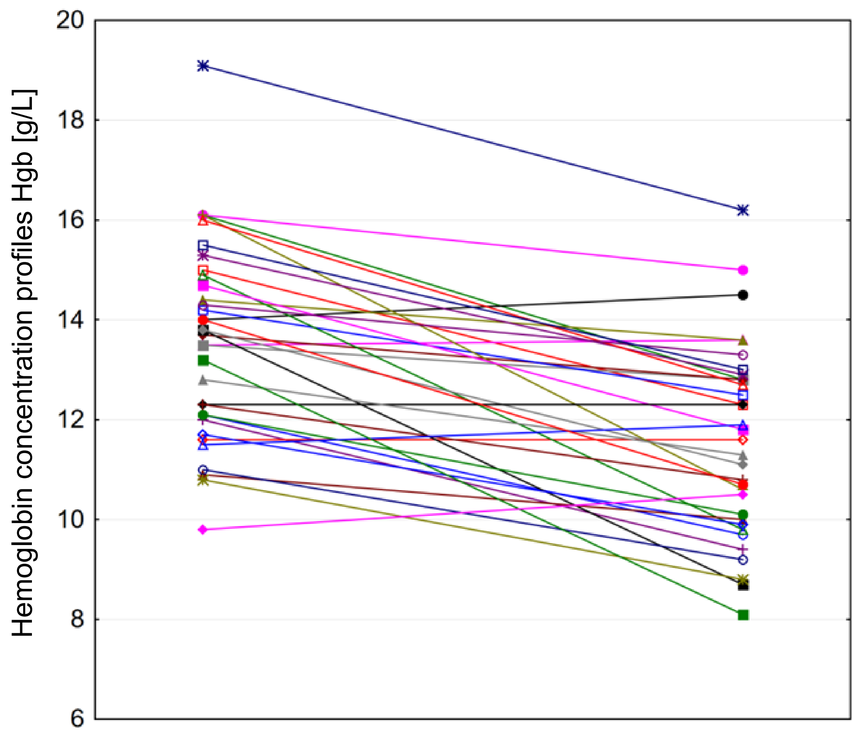

Fig. 4. Change in hemoglobin concentration during the first 4 weeks of therapy in individual patients.

Any other important side effects were observed during therapy. However, due to the risk of potential drug interactions in one patient, treatment with amiodarone had to be stopped prior to initiation of treatment, and after 8 weeks of wash-out, SOF / LDV / RBV therapy was performed without complications and another patient needed a change in existing epilepsy therapy.

Conclusions

1. **In KTR, the new anti HCV therapies with SOF±LDV and RBV are characterized by 100 % effectiveness and very good safety profile.**
2. **The decrease of Hb concentration resulting from RBV administration, however expected, in some cases (11% of patients) was the indication for discontinuation of RBV therapy.**
3. **In patients treated with RBV and co-therapy within new DAA regimens, close monitoring of blood Hb concentration and early RBV dose reduction is necessary.**

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