# The effects of calcineurin inhibitors on sperm DNA fragmentation in male kidney transplant recipients

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## *Objectives:*

Successful kidney transplantation (KT) can significantly improve spermatogenic function in uremic patients. In the last few decades, low early rejection rates and excellent short-term kidney allograft outcomes are obtained with different combinations and dosages of calcineurin inhibitors (CNI, cyclosporine-CsA and tacrolimus-Tac), corticosteroids and antiproliferative drugs. Generally, these drugs commonly used after KT have not been associated with adverse effects on patient spermatogenesis or with teratogenic effects on their offspring. Some studies imply that CsA is a potentially gonadotoxic drug that produced adverse effects on reproductive capability in experimental models as well as in humans. In a recent study Tac has been induced mild changes of spermatogenesis without histological evidence of testicular injury in rats subjected to unilateral nephrectomy. Therefore, this study aimed to compare effects of CNIs on sperm production capacity and sperm DNA defects in kidney transplant recipients.

## *Methods:*

This observational, cross-sectional study included 38 consecutive male kidney transplant patients who had not azoospermia. Seminal ejaculates were examined for sperm DNA fragmentation damage by TUNEL assay using a terminal deoxynucleotidyl transferase–mediated fluorescein-TUNEL assay with an In Situ Cell Death Detection Kit, Roche. Also semen analyses were performed.

## *Results:*

Of patients, 27 patients received Tac treatments and 11 patients received CsA together with mycophenolate and prednisolone. The mean age (33.7±8.2 vs. 34.8±8.3 years), disease starting age (26±8.6 vs. 25.9±8.8 years), dialysis starting age (27.1±9 vs. 26.5±10 years), dialysis duration (56.9±63.9 vs. 49.3±46 months), transplantation duration (32.3±23.2 vs. 42.2±28.3 months), transplant age (28.3±11.6 vs. 34.9±20.8 years) and immunosuppressive treatment duration (32.9±22.8 vs. 41.8±28.2 months) of CsA and Tac groups were comparable. There was no difference in semen volume (2.36±0.5 vs. 3.11±1.3 mL), sperm concentration (48.9±41.2 vs. 63.4±53.1 $10^6$/mL), total sperm count (102.7±82.2 vs. 171.8±148 $10^6$), total motility ((48.7±24% vs. 54.1±24.4%), progressive motility ((34±21.2% vs. 43±20.1%), normal morphology ((3.2±2% vs. 3.7±2.2%) and DNA fragmentation ((17.0±6.4% vs. 17.3±11.7%) between the CsA and Tac groups, respectively ($p>0.05$). In paternity status of semen analysis, oligozoospermia (O), asthenozoospermia (A) and teratozoospermia (T) ratios of both groups were similar ($p>0.05$, Table 1). Number of patients who have children was 1 in the CsA group and 13 in the Tac group ($p<0.05$). The ratio of the inability to have children in the CsA group were higher than that of the Tac group (90% vs. 48.1%, $p<0.05$). When 20% was accepted for threshold value for sperm DNA fragmentation, patients in the CsA group have slightly higher fragmentation rate in their spermatozoa than the Tac group (36% vs. 22%). There was no significant correlation DNA fragmentation with other studied parameters in all study population.

## *Conclusions:*

Our study showed that motility and morphology of the spermatozoa between CNIs were similar, but the patients receiving CsA could have higher sperm DNA fragmentation rate.

*Table 1. The paternity status of the both groups*

| Groups | OAT | AT | OT | O | A | T |
|---|---|---|---|---|---|---|
| CsA, n | 1 | 1 | 1 | 2 | 4 | 4 |
| Tac, n | 4 | 2 | 1 | 5 | 8 | 11 |


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