

The effect of smoking on the kidneys

Graham Cope outlines the ways in which smoking impairs both kidney function and prognosis in kidney disease. Knowledge of the negative impact of cigarette smoking in renal disease can assist the nurse in educating and supporting patients in smoking cessation.

■ cigarette smoking ■ chronic kidney disease ■ smoking cessation ■ nicotine ■ cancer

Smoking is known as a major risk factor for lung cancer and heart disease. However, recent evidence shows that it is also a significant cause of renal disease, that it reduces the efficacy of treatment and is the main preventable reason for kidney transplant failure.

Chronic kidney disease

The increasing worldwide prevalence of chronic kidney disease (CKD) and the growth in the number of patients reaching end-stage kidney disease have prompted nephrologists to identify factors that increase the risk of renal disease. In recent years it has become clear that cigarette smoking is an important independent risk factor for CKD and that it has deleterious effects on renal function (Hallan and Orth, 2011).

Although the general effect of smoking on CKD is not in doubt, there is some uncertainty as to whether smoking affects men and women alike and if age of disease onset is important. It is also not known if the duration and amount of smoking are significant in the progression of renal disease (Hallan and Orth, 2011). Dose-response relationships have been demonstrated for certain aspects of renal function decline, with the number of cigarettes smoked correlating with the levels of proteinuria (Briganti et al, 2002) and to low estimated glomerular filtration rate (Ejerblad et al, 2004), both of which are strong indicators for progression to kidney failure.

CKD is associated with cardiovascular disease and diabetes, both of which are linked to cigarette smoking. The complications of diabetes, such as neuropathy and retinopathy, are more severe and have a poorer prognosis in smokers than

non-smokers. It follows that smoking enhances the progress of diabetic nephropathy from microalbuminuria to persistent proteinuria, and advances the progression to end-stage kidney disease (Obert et al, 2011). Cigarette smoking has also been correlated with the progression of a number of renal conditions, notably lupus nephritis, immunoglobulin A (IgA) nephropathy, and hypertensive and autosomal dominant polycystic kidney disease (Gombos et al, 2010).

Renal cancer

Smoking is a significant risk factor for renal cancer, particularly renal cell carcinomas. There is a higher mortality rate in heavy smokers and a reduced rate of disease in those who have quit for a period of years; suggesting that cancer progression may be more aggressive in smokers (Tsivian et al, 2011).

The same study found current smokers had a higher incidence of metastatic disease and lymph node involvement, and more progressive disease (Tsivian et al, 2011). Smokers with less than 10 years' cigarette smoking had a marginally increased risk of advanced disease compared to non-smokers at 6%, whereas those who had smoked for 10–20 and 20–30 years increased their risk by 44% and 71% respectively.

Smoking is a risk factor for cancers elsewhere in the urogenital tract, with tobacco users being at higher risk of bladder cancer, mainly because of an increased incidence of transitional cell carcinoma, (Freedman, 2011). However, paradoxically, one study found that non-smokers had significantly more high-grade tumours at presentation than non-smokers (Lammers et al, 2011). Prostate cancer is also more common in smokers, with a higher incidence of prostate cancer-specific mortality and recurrence (Walsh, 2012).

Effect on RRT

Smoking affects treatment for CKD; current smokers have a hazard ratio of 2.6 for future renal

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replacement therapy (RRT) and the risk increases with greater cigarette consumption. Smokers also have a poorer outcome from dialysis treatment, with a perceived lower quality of life and an increased prevalence of depression (Østhus et al, 2010). There is again a higher risk of mortality in dialysis patients who smoke, with no perceptible increased incidence of cardiovascular disease (Liebman et al, 2011).

Renal transplantation

Research has shown that cigarette smoking is detrimental to renal transplantation, both to the patient and the graft survival (Agarwal et al, 2011), with a significantly increased risk of rejection within one year. Interestingly, smoking by the donor also increases the risk of rejection. Serum creatinine levels at 3 years after engraftment correlate with the intensity and duration of smoking by the recipient, as does the increased risk of graft failure (Hurst et al, 2011).

Mechanisms

Cigarette smoke is a complex mixture of nicotine, carbon monoxide, heavy metals, carcinogens and reactive oxygen species. Nicotine is the addictive substance that compels smokers to continue their habit, even in the knowledge that smoking is irrevocably damaging their health. Nicotine and other tobacco products are absorbed into the bloodstream and enter the brain in a matter of seconds, from where they continue to circulate throughout the body: constricting blood vessels, hardening arteriole and capillary walls, increasing the deposition of atheroma and elevating blood pressure (Leone, 2011).

The immune system is suppressed by smoking, reducing its ability to fight infection and eradicate cancer cells, and also reducing the rate and efficiency of wound healing. The activity of leukocytes and the production of many cytokines and growth factors are disrupted by smoking, including the activation of angiotensin II, endothelin-1, and TGF- α 1, which are important in producing renal fibrosis (Orth and Hallan, 2008).

There are specific nicotinic receptors on the membranes of many cell types, and a recent study by Hallan and Orth (2011) showed the presence of nicotinic receptors on the walls of mesangial cells (specialized cells around blood vessels in the kidneys). Stimulation of these receptors results in proliferation and enhanced extracellular matrix production, which directly affects blood vessel constriction. This increases the pressure inside the kidney and can lead to glomerular and tubular damage, and then to chronic disease (Obert et al, 2011).



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Smoking is an important risk factor for kidney disease

Carbon monoxide generated by the burning of tobacco combines with erythrocytes to form carboxyhaemoglobin, which reduces the oxygen carrying capacity of the blood, thus hampering tissue reconstruction and further inhibiting wound healing. Cigarette smoke is also a source of heavy metals, such as cadmium, and lead which are toxic to renal tissue at very low concentrations. The metals accumulate in kidney tissue more than in any other organ and contribute to tubular and glomerular dysfunction (Mordata et al, 2004).

Free radicals and antioxidants

Tobacco smoke is a concentrated source of reactive oxygen species, also known as free radicals, such as peroxide and superoxide. These are short-living, highly-reactive chemical species, which cause damage to macromolecules, such as membrane lipids, glycoproteins and DNA. Such damage increases the probability of genetic mutation, which may result in cancer. Normally reactive oxygen species are inhibited by natural antioxidants such as vitamin C and E, but dietary intake of these nutrients is reduced in smokers (Jain et al, 2009).

A number of large molecular weight carcinogens are present in cigarette smoke, notably polycyclic aromatic hydrocarbons, which have been implicated in causing mutations in cancer-related genes. One such gene is p53, which can potentially lead to the initiation and acceleration of the growth of cancer cells.

Genetics play an important role in determining susceptibility to smoking-related kidney disease. Many genes are involved, and polymorphisms will influence the magnitude of the nephrotoxic effect of smoking. The susceptibility of individuals will be





Vicky Lush

Smokers on dialysis have a poorer quality of life

influenced by genetic expression and their ability to neutralize tobacco toxins and combat the harmful effects of nicotine and the carcinogens (Kroeger et al, 2011).

Recipients of kidney transplants have drug-induced immunosuppression, so have a greater risk of infection and reduced wound healing. If the patient continues to smoke post-operatively then these effects are magnified. Although evidence suggests renal transplantation is a strong incentive to quit smoking, these data are based on self-reported smoking habits and may be incorrect as they are subject to bias and misreporting (Banas et al, 2008).

Information gathering

Smoking is an important risk factor for the development, progression and treatment of CKD, so accurate information is required from all patients at the beginning of and at regular stages throughout treatment. There is anecdotal evidence that smokers will reduce their smoking at the beginning of a clinical treatment but will resume their usual habit if not regularly questioned.

Given the increasingly anti-social nature of smoking, many patients believe that their treatment will be compromised or withheld if they continue to smoke, so many, up to 25% of smokers, will deny smoking when questioned (Payne and Southern, 2006). As all research into smoking and CKD has relied on self-report data, there will be inaccuracies in the data collected, and this may give rise to the uncertainty about the relationships between gender, smoking duration and kidney disease. This problem highlights the need for biochemical tests to verify self-report. Expired-air carbon monoxide monitoring is a popular method however, it is not specific to tobacco

smoke and owing to CO's short half-life (the time it remains in the body), it only monitors smoking habit over a period of a few hours. An alternative is cotinine testing, a metabolite of nicotine, which is only generated by nicotine itself and it has a long half-life such that it can be used to monitor smoking over a period of days. Simple, point of care tests are available that can be carried out by nurses in the clinical setting (Cope et al, 1996).

How to help

Once smokers have been identified it is not enough to tell them they should quit. Many smokers resent this approach and it serves to reduce smoking habit very little. The personalization of advice and the tailoring of help and support have been shown to be much more effective. The biochemical tests, particularly for cotinine, can be used to explain why smoking is particularly harmful to their kidney disease. Feedback of information from the test helps to engage with the patient, while regular testing reiterates the message and shows a sense of caring and support (Barnfather et al, 2005).

The patient should be directed towards national support services (*Box 1*) and be given encouragement to attend local smoking cessation services. This could be enhanced by the nursing or support staff booking an appointment with the service, which helps to improve attendance. Training of smoking cessation counselling to nursing staff improves the efficiency and confidence to engage patients in discussions.

Integrating the correct identification of smokers and smoking cessation counselling will improve the efficacy of treatment, enhance the patient's ability to cope with renal replacement therapy and has been shown to be the most cost-effective means of reducing the complications of treatment of chronic kidney disease (Orth and Hallan, 2008). **JRN**

References

- Agarwal PK, Hellemons ME, Zelle DM et al (2011) Smoking is a risk factor for graft failure and mortality after renal transplantation. *Am J Nephrol* **34**(1): 26–31
- Banas MC, Banas B, Wolf J et al (2008) Smoking behaviour of patients before and after renal transplantation. *Nephrol Dial Transplant* **23**(4): 1442–6
- Barnfather KD, Cope GF, Chapple IL (2005) Effect of incorporating a 10 minute point of care test for salivary nicotine metabolites into a general practice based smoking cessation programme: randomised controlled trial. *BMJ* **331**(7523): 999–1001

Box 1. NHS smoking helpline

Call Smokefree: 0800 022 4 332

Contact advisors online: <http://smokefree.nhs.uk/>

- Briganti EM, Branley P, Chadban SJ, Shaw JE, McNeil JJ, Welborn TA, Atkins RC (2002) Smoking is associated with renal impairment and proteinuria in the normal population: The AusDiab kidney study. *Am J Kidney Dis* **40**(4): 704–12
- Cope GF, Nayyar P, Holder R, Gibbons J, Bunce R (2000) A simple near-patient test for nicotine and its metabolites in urine to assess smoking habit. *Clin Chim Acta* **256**(2): 135–49
- Ejerblad E, Fored CM, Lindblad P et al (2004) Association between smoking nationwide population-based and chronic renal failure in a case-control study. *J Am Soc Nephrol* **15**(8): 2178–85
- Freedman ND, Silverman DT, Hollenbeck AR, Schatzkin A, Abnet CC (2011) Association between smoking and risk of bladder cancer among men and women. *JAMA* **306**(7): 737–45
- Gombos P, Langer RM, Korbely R, Varga M, Kaposi A, Dinya E, Müller V (2010) Smoking following renal transplantation in Hungary and its possible deleterious effect on renal graft function. *Transplant Proc* **42**(6): 2357–9
- Hallan SI, Orth SR (2011) Smoking is a risk factor in the progression to kidney failure. *Kidney Int* **80**(5): 516–23
- Hurst FP, Altieri M, Patel PP et al (2011) Effect of smoking on kidney transplant outcomes: analysis of the united states renal data system. *Transplantation* **92**(10): 1101–7
- Jain A, Agrawal BK, Varma M, et al (2009) Antioxidant status and smoking habits: relationship with diet. *Singapore Med J* **50**(6): 624–27
- Kroeger N, Klaffe T, Birkhäuser FD, et al (2011) Smoking negatively impacts renal cell carcinoma overall and cancer-specific survival. *Cancer* **118**(7): 1795–802
- Lammers RJM, Witjes WJP, Hendricksen K, Caris CTM, Janzing-Pastors MHC, Maria HC (2011) Smoking status is a risk factor for recurrence after transurethral resection of non-muscle-invasive bladder cancer. *Eur Urol* **60**(4): 713–20
- Leone A (2011) Smoking and hypertension: independent or additive effects to determining vascular damage? *Curr Vasc Pharm* **9**(5): 585–93
- Liebman SE, Lamontagne SP, Huang LS, Messing S, Bushinsky DA (2011) Smoking in dialysis patients: a systematic review and meta-analysis of mortality and cardiovascular morbidity. *Am J Kidney Dis* **58**(2): 257–65

Key points

- Cigarette smoking is a significant risk factor for chronic kidney disease
- Smoking increases blood pressure and hardening of blood vessels
- Nicotine is an immunosuppressive
- Carcinogens such as polycyclic aromatic hydrocarbons are present in smoke
- Reactive oxygen species causes tissue and macromolecular damage

Mordata WI, Sobh MA, El-Defrawny MM (2004) The exposure of cadmium, lead and mercury from smoking and its impact on renal integrity. *Med Sci Monitor* **10**(3): CR112–6

Obert DM, Ping H, Pilkerton ME, Feng W, Jaimes EA (2011) Environmental tobacco smoke furthers progression of diabetic nephropathy. *Am J Med Sci* **34**(2): 126–30

Orth SR, Hallan SI (2008) Smoking: a risk factor for progression of chronic kidney disease and for cardiovascular morbidity and mortality in renal patients—absence of evidence or evidence of absence? *Clin J Am Soc Nephrol* **3**(1): 226–36

Østhus TBH, Dammen T, Sandvik L, Bruun CM, Nordhus IH, Os I (2010) Health-related quality of life and depression in dialysis patients: Associations with current smoking. *Scand J Urol Nephrol* **44**(1): 46–55

Payne CE, Southern SJ (2006) Urinary point of care test for smoking in the pre-operative assessment of patients undergoing elective plastic surgery. *J Plast Reconstr Aesthetic Surg* **59**(11): 1156–61

Tsivian M, Moreira DM, Caso JR, Mouraviev V, Polascik TJ (2011) Cigarette smoking is associated with advanced renal cell carcinoma. *J Clin Oncol* **29**(15): 2027–31

Walsh PC (2012) Smoking and prostate cancer survival and recurrence. *J Urol* **187**(1): 141–2

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