SPIRO-CKD Newsletter

A Randomised Multicentre Open Label Blinded End Point Trial to Compare the Effects of Spironolactone to Chlortalidone on Left Ventricular Mass in Stage 2 and Stage 3 Chronic Kidney Disease

Results Issue – January 2021

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Welcome to the final issue of the SPIRO-CKD Newsletter

The SPIRO-CKD Trials Team would firstly like to thank everyone who has been involved in the trial for their hard work.

The trial has certainly had its challenges, but we are proud of what everyone has achieved.

We have been in the going through the data collected so the team can analyse the results.

In this edition, we will provide you with the results of the trial and explain what it means going forward.

SPIRO-CKD Recap

What was the purpose of the trial?

Stage 1 to 3 chronic kidney disease (CKD) affects more than 10% of the population in developed countries. People who suffer with CKD are at an increased risk of developing hardening of the blood vessels (arterial stiffness), which can increase the risk of heart disease and strokes. Although it is unlikely to progress to end-stage kidney disease there is an increased risk of cardiovascular disease.

Spironolactone is a drug used to treat people who have high blood pressure, heart disease or liver disease and has been suggested to improve heart function, reduce the hardening of the blood vessels, and improve blood pressure.

Chlortalidone is a drug that is used to treat blood pressure but works in a different way to spironolactone.

The SPIRO-CKD Team investigated whether spironolactone or chlortalidone could reduce the size and weight of the heart (left ventricular mass), which would decrease the risk of heart disease.

What was the aim of the trial?

The aim of the trial was to compare the effects of spironolactone and chlortalidone on heart and blood pressure function in non-diabetic participants who suffer stage 1 to 3 CKD with high blood pressure. The results may provide information on the best way to treatment for these participants.

What we think would happen

The SPIRO-CKD research team believed that spironolactone would be better than chlortalidone in decreasing the size and weight of the heart due to the type of medication spironolactone is. The aim of the trial is to find out if spironolactone acts in a unique way to improve heart function and blood pressure function or whether these effects are due to the lower blood pressure.

Methods

Participants recruited into the trial were 18 years and over, had stable CKD and were taking medication to control blood pressure.

The trial involved 4 centres across the UK (Birmingham, Cambridge, Edinburgh, and London). Participants attended clinic 8 times for follow-up.

Medication was taken orally for 40 weeks in total. Participant follow-up was completed at 46 weeks.

SPIRO-CKD Results

Study participants

Between June 2014 and December 2016, a total of 154 participants were recruited into the trial.

	Spironolactone group	Chlortalidone group
How many participants were in the group?	77	77
How many participants did not complete the trial?	8	8
How many participants remained on full dose of medication until the trial finished?	50	52
How many participants changed their medication to half-dose?	12	4
How many participants stopped medication completely?	11	19

What did the results show?

In participants with early stage, non-diabetic CKD, left ventricular mass and blood pressure both decreased with spironolactone and chlortalidone, however no difference was found between treatments after participants took medication for 40 weeks.

There was also no difference observed between spironolactone and chlortalidone with:

- Left ventricular shape, size, weight or function
- Hardening of the blood vessels
- Markers of kidney and heart function (Albumin Creatinine Ratio (ACR) and NT-pro-BNP)

Both treatments were well tolerated in the participants recruited with a low number of participants reporting serious side effects.

Conclusion

The SPIRO-CKD Team thought that treating participants who had early stage CKD and high blood pressure with spironolactone would decrease the size and weight of the heart more when compared to chlortalidone. But the SPIRO-CKD Trial could not prove that spironolactone was better than chlortalidone. It was also found that there was no difference between spironolactone or chlortalidone in decreasing blood pressure or hardening of the blood vessels .

The SPIRO-CKD Team observed that there may be a link between the decrease in LV mass and decrease in blood pressure. However, to confirm this link, more research in this area is needed.

Message from the Chief Investigator

Thank you very much for taking part in SPIRO-CKD. We know the trial was demanding in some ways. The trial was completed successfully and both drugs were effective in lowering blood pressure. To our slight surprise, we found no convincing evidence that spironolactone (our test drug) was better to chlorthalidone (our control drug) in reducing the size of the heart or any of the other end points. It was however, better tolerated with fewer side effects.

Based on these results, we can recommend both drugs for possible use in kidney disease but cannot claim any special effects of spironolactone. This is an important finding as there are a number of drug companies currently making new versions of spironolactone.

The SPIRO-CKD Trials Team

Queen Elizabeth Hospital Birmingham	Birmingham Clinical Trials Unit
Chief Investigator: Prof. Jon Townend John.townend@uhb.nhs.uk	**Trial Email:** SPIRO-CKD@trials.bham.ac.uk
SPIRO-CKD Website: www.birmingham.ac.uk/spirockd	

SPIRO-CKD Trials Office:

SPIRO-CKD Trial Office
Birmingham Clinical Trials Unit (BCTU)
Institute of Applied Health Research
College of Medical and Dental Sciences
Public Health Building
University of Birmingham
Edgbaston
Birmingham
B15 2TT

Telephone: (0121) 415 8445
Fax: (0121) 415 9135