THE MANAGEMENT OF PATIENTS WITH ELEVATED DNA FRAGMENTATION TEST RESULTS

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Introduction

Testing for sperm DNA damage (fragmentation) is a recent tool available to assist subfertility management. It has been used in Galway Fertility since 2011 to add to the information used to advise couples on their treatment plans. The aetiology of this damage is often unclear, but has been linked to a number of factors including lifestyle, (such as diet, exercise, smoking etc.) which contribute to the damaging effects of temperature or oxidative stress, or limit the bodies ability to repair such damage (Sakkas and Alvarez 2010; Wright et al. 2014). Galway Fertility discuss lifestyle improvements with all male patients to identify areas for improvement.

Methodology

A retrospective analysis of 517 patients attending Galway Fertility, where sperm DNA damage was tested by SPZ Lab on frozen semen samples, were included in this study. Of the 517 samples, 69 had a DFI above the 30% threshold (Evenson and Wixon 2008) indicating a low chance of achieving a spontaneous pregnancy or successful IUI. Some were tested at initial fertility assessment stage, and others after failed ART. Potential lifestyle improvements (NICE Guidelines 2004) were discussed in detail with all of the men where the DFI was above 20% to identify areas for improvement, including a referral to a nutritionist where this was deemed appropriate. A repeat semen analysis and test for sperm DNA damage was carried out to measure the effects of the lifestyle changes (ranging from 2 months to 15 months later). Subsequent treatment plans were drafted based on other factors including the womens' age, aetiology, previous treatments, and other contributory factors. ART included Ovulation Induction, IUI, IVF and ICSI.

Fig 1. DNA Fragmentation Index (DFI)
Of the 517 samples tested,
49.1% had a normal result of <15%DFI,
35.2% had a result >20%DFI

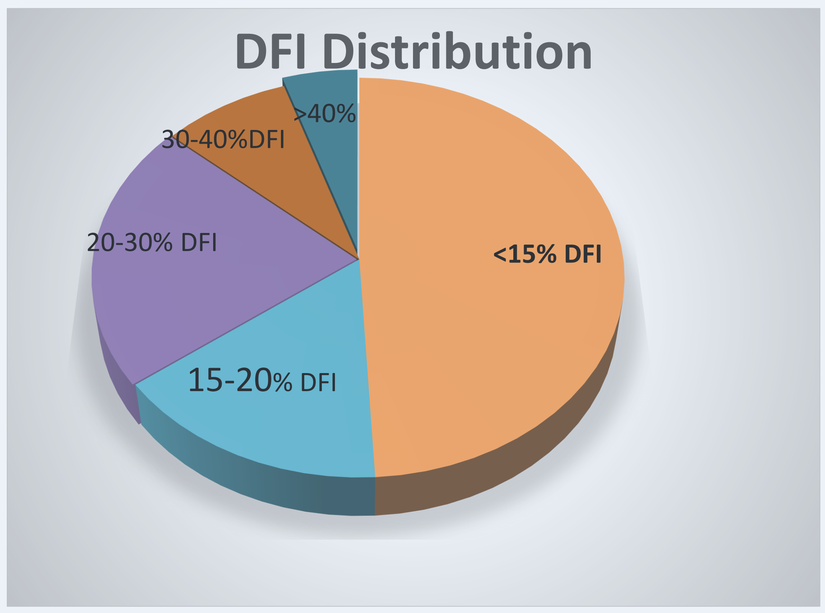

Fig 2.	>10% points Decrease in DFI	<10% Decrease, or no change in DFI
n	13	14
Average Decrease (%)	35.6 to 18.5	29.8 to 24.6
Average Female age	36.2	37.1
Spontaneous Preg	3 (all ongoing) (23%)	1 (ongoing) (7%)
Underwent ART:	9	10
->Positive hCG	7 (77.8%)	3 (30%)
->Clinical Preg	6 (66.7%)	3 (30%)
->Ongoing Preg	5 (55.6%)	1 (10%)

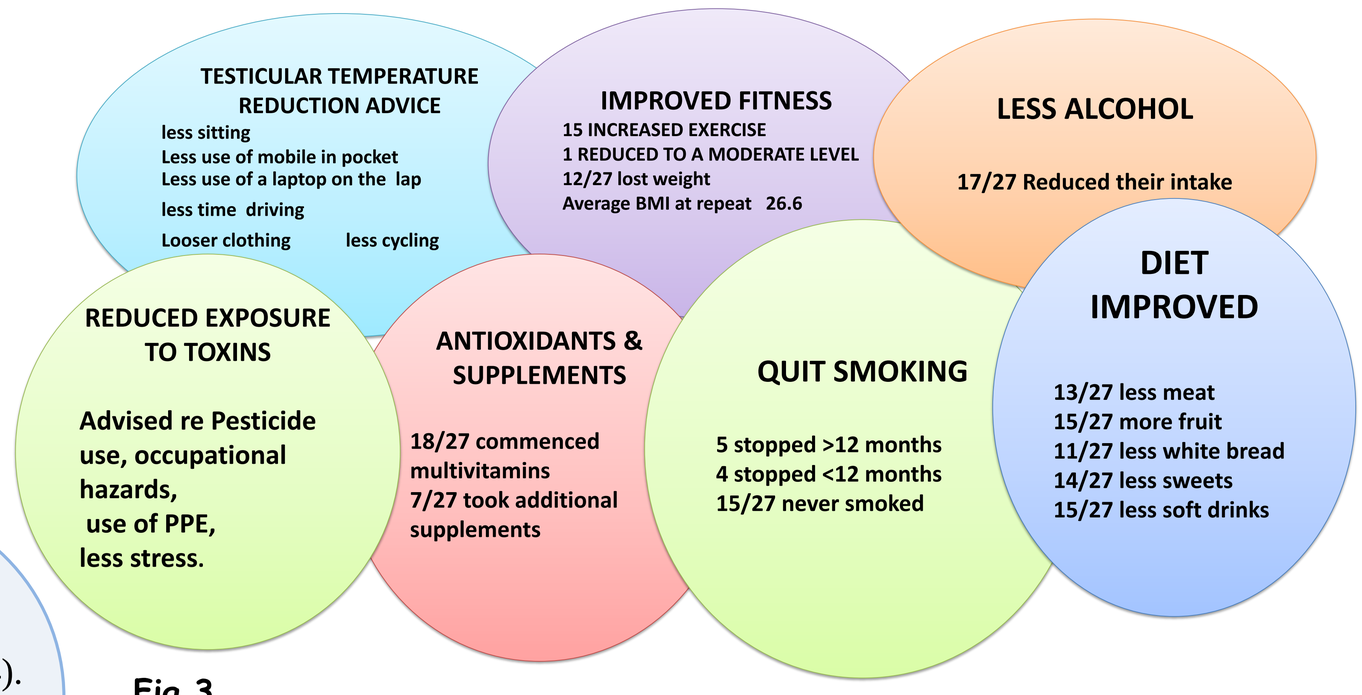

Fig 3.
Details of the lifestyle advice and changes made. These were very heterogeneous and self monitored, and the health of the individuals prior to the changes was very diverse. No correlations could be drawn from the limited data set, without a control group.

Results & Outcomes

To date 27 men have had repeated semen analysis and DFI test. The average DFI level was reduced from 32.6% to 21.6% (P<0.0001, Fig. 4). The largest individual reduction was from 53.4% to 17.6%.

A significant improvement was also noted for sperm motility which increased from 48.3% to 56.1% (P=0.011). Sperm motility showed the highest correlation with DFI (r=-0.30, P=0.0167,). A significant change was not found for sperm morphology or for sperm concentration.

Five couples have not been treated (ART) at the time of data analysis. Among the 13 couples where DFI was reduced by more than 10% points, 3 couples achieved a spontaneous pregnancy and 9 had ART treatment. Five couples had ongoing pregnancies (55.6% clinical pregnancy/cycle). Two did not achieve pregnancy and two additional couples had a positive hCG but later had a miscarriage. (Fig 2)
Among 10 couples where the reduction in DFI was less than 10% points, 1 couple achieved a spontaneous pregnancy. Among 9 couples receiving ART, only one achieved an ongoing pregnancy (10.0% clinical pregnancy/cycle) and two couples had a positive hCG but no ongoing pregnancy.

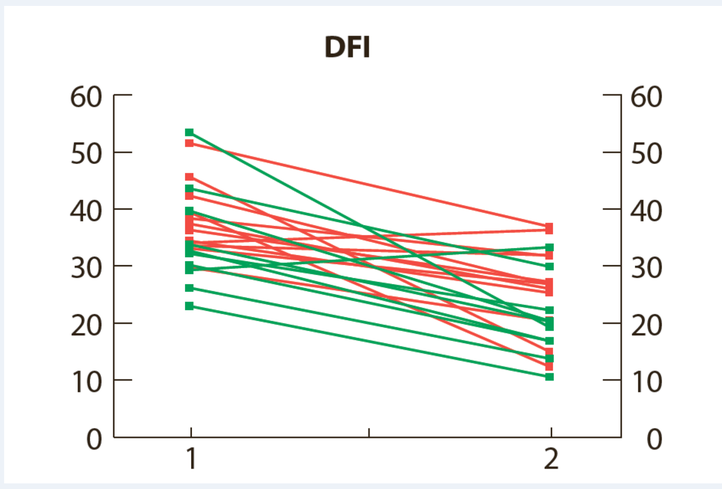

Fig 4.
Absolute change in DFI for all 27 individuals that repeated the DFI test following lifestyle advice. The average DFI level was reduced from 32.6% to 21.6% (P<0.0001).
Green lines represent ongoing Pregnancies achieved after the repeat test, both spontaneous and with ART.
Red lines represent those with no pregnancies yet.

Conclusion

From this data set it is not possible to draw correlations between the actual changes made and the reductions in DFI, improvement in sperm motility, or their reported improvement in fitness. However the results would suggest that further research is warranted to evaluate which factors are more important.
Galway Fertility have found that there is better adherence to the pre-conception advice by the men when they have the feedback of a measurable test in a clinical setting. Evidence that these changes can improve pregnancy (Wright et al 2014), and the side effects of improved health, are strong motivational factors for the men.

References

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