Barthel score, change in Barthel score, and survival time of patients in hospice with cancer

	Sample 1 (n=93)	Sample 2 (n=104)	P value (Mann-Whitney U test)
Mean (range) Barthel score at admission	66 (3-100)	58 (2-100)	0.056
Median (range) length of stay (days)	18 (5-104)	19 (3-86)	0.82
Median (range) survival (days)	35 (5-473)	27 (3-349)	0.2
Median (interquartile range) change in Barthel index:			
No loss of points	56 (23-137) (n=50)	68 (19-128) (n=41)	0.91
1-9 points lost	32 (17-56) (n=24)	31 (15-45) (n=39)	0.51
⩾10 points lost	14 (11-20) (n=19)	15 (6-20) (n=24)	0.65
P value (Kruskal-Wallis test)	<0.001	<0.001	–

measure, but this has not been supported.[4] Despite this, half of patients with advanced cancer who lose 10 or more points per week die within two weeks (95% confidence interval 8.6 days to 19.4 days), and three quarters are dead at three weeks. In contrast, 50% of patients in whom the weekly score does not deteriorate survive for two months (35.2 days to 76.8 days).

Although Barthel score at admission correlated with overall survival, no differences in scores on admission were found among the three groups in either sample (sample 1, P = 0.08, and sample 2, P = 0.74, Kruskal-Wallis; see table on website). Admission score therefore cannot be used to determine pattern of subsequent change and hence to estimate survival more accurately.

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Drug points

Apparent interaction between warfarin and levonorgestrel used for emergency contraception

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Emergency contraception with progestogen only (two doses of levonorgestrel 0.75 mg given 12 hours apart and within 72 hours of unprotected intercourse) is better tolerated and more effective than the combined oestrogen-progestogen (Yuzpe) regimen.[1] Furthermore, treatment with progestogen only may be preferable to the Yuzpe regimen in women with a known thrombophilic defect or history of thromboembolic events. For women receiving warfarin, drug information cites either no interaction between progestogens and warfarin[2] or a reduction in anticoagulant effect.[3] We describe an enhanced anticoagulant effect of warfarin after giving a woman levonorgestrel for emergency contraception.

A 35 year old woman with familial type 1 (quantitative) antithrombin deficiency and a history of extensive deep venous thrombosis and pulmonary thromboembolism, attended the clinic after an episode of unprotected intercourse. She was receiving warfarin 7 mg daily for anticoagulation but no other drugs. Her international normalised ratio was 2.1, which was within the therapeutic range (2.0-3.0). She requested emergency contraception. After counselling, she declined the insertion of an intrauterine contraceptive device, preferring the progestogen only regimen. Her international normalised ratio was rechecked three days later and was reported as 8.1. She was advised to discontinue warfarin treatment for two days, at which point her international normalised ratio was 2.5, and then to restart it at a dose of 5 mg once daily. No haemorrhagic problem occurred.

One possible explanation for this enhanced anticoagulant effect is the displacement of warfarin by levonorgestrel from the F1S binding site of human α_1-acid glycoprotein, the main transport protein for drugs in plasma.[4] The variant of the F1S binding site comprises part of the F1S/A phenotype of α_1-acid glycoprotein, which is encountered in 50% of the population.

Thus women receiving warfarin treatment may be at risk of an interaction between warfarin and levonorgestrel if they are prescribed the progestogen only regimen because of its apparent safety. The manufacturer of levonorgestrel (Wyeth) has not received any reports describing such an interaction with warfarin. This potential interaction requires prompt investigation, particularly in light of recommendations that emergency contraception be made available over the counter.[5] If patients are fully anticoagulated with warfarin, the conventional Yuzpe regimen may be effective without being associated with any increased risk of venous thromboembolism.

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