DOSE OF THERAPEUTIC EXERCISE NEEDS OUR ATTENTION

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KEY POINTS

1. Exercise is accepted as a fundamental component of the treatment of many health conditions.
2. Despite a known dose-response relationship between exercise and health benefits, effective exercise doses remain largely unknown.
3. To advance development of ‘precision’ or ‘personalized’ physiotherapy practice, identification of evidence-based effective doses of our therapeutic interventions is critical.

Background and objective

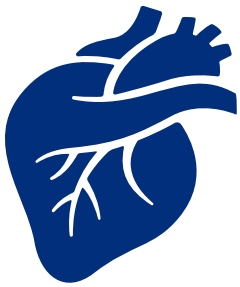
Regaining walking ability is a common goal of individuals after stroke. Stroke rehabilitation guidelines consistently recommend both aerobic exercise and task-specific therapy to enhance walking recovery. While the concept of 'dose' is central to effective prescription of drugs, it has not been adequately considered in exercise prescription.
The primary objective of the DOSE (Determining Optimal Post-Stroke Exercise) trial was to compare the effectiveness of 2 higher doses of exercise to usual care in improving walking recovery after stroke.

Methods

The DOSE Trial was a Phase II, multi-centre, assessor-blind, randomized control trial. 75 adults within 10 weeks post-stroke, and with lower extremity hemiparesis and walking speed <1.0 m/sec, were randomized into one of three 4-week physiotherapy treatment groups:

- *USUAL CARE* (1 hour, 5 days/week)
- *DOSE1* (1 hour, 5 days/week, with targets of 60 minutes and 2000 steps per session)
- *DOSE2* (2 hours, 5 days/week with targets of 120 minutes and 4000 steps over two daily sessions).

> *"a movement away from a 'one size fits all' approach to more precision in the way we prescribe exercise*[1]



Fitbit One™ step counters and Alpha Mio™ heart rate monitors were used to measure step counts and time spent over 40% heart rate reserve (HRR) per session, respectively. At program completion, and 6 and 12-month post-stroke, linear regression was used to analyze changes in the primary outcome (6-minute walk test, 6MWT) and secondary outcomes of walking speed (5-meter walk test, 5MWT), quadriceps strength (handheld dynamometer, HHD), Berg Balance Scale (BBS), depression (patient health o questionnaire, PHQ), and quality of life (EQ-5D-5 L).

Results

- Both *DOSE 1* (61 m; 95% CI, 9–113, P=0.02) and *DOSE 2* (58 m; 95% CI, 6-10, P=0.03) mean pre-post 6MWT distances significantly exceeded that of *USUAL CARE* (50 m)
- Similarly, improvements in quality of life of the experimental groups compared to *USUAL CARE* also exceeded the minimally clinically important difference (MCID: 0.102) by a similar magnitude (mean changes were 0.11 [P=0.001] for both *DOSE1 and DOSE2* groups).
- Importantly, gains in 6MWT were retained at 12-month follow-up. No between-group differences were found for HHD, BBS, or PHQ.
- Each group fell short of session duration targets with average total durations of 44±12 minutes for *USUAL CARE*, 52±5 minutes for *DOSE1,* and

104±15 minutes for *Dose2*. Time in daily sessions at >40% HRR were about 25% of each *USUAL CARE* session and about 50% of each *Dose1* and *Dose2* session were spent in aerobic training zones.

- Both *DOSE 1* and *DOSE 2* exceeded daily session step counts targets, averaging 2169±1106 steps for *DOSE 1* and 4747±2083 steps for *DOSE2,* whereas *USUAL CARE* averaged only 580±440 steps.

Limitations

- The small sample sizes per group necessitated collapsing DOSE1 and DOSE2 data in order to conduct longitudinal modelling across time points (program completion, 6 and 12-month follow-up). This compromised meeting the primary objective of determining whether 2 higher doses were more effective than usual care at improving walking recovery post-stroke.

Clinical Implications

Phase IIb trials, such as the DOSE trial, often involve determining the optimal dose for safety and effectiveness.[2] Although this trial fell short of pinpointing the 'optimal exercise post-stroke', the findings supported a dose-response relationship between exercise and clinical outcomes. A 2014 meta-analysis reported a positive relationship between stroke rehabilitation and extent of motor improvement but defined dose as total time scheduled for therapy.[3] In contrast, in the DOSE trial, affordable wearable technology recorded step counts, thus incorporating both time and intensity (number of repetitions) into the operational definition of dose and facilitating more precise prescription.

Targets of 2000 steps for DOSE1 and DOSE2 session training far exceeded the average number of 357 steps taken in typical stroke rehabilitation sessions, a dose deemed inadequate to drive the neural changes required to promote function post-stroke.[4] The DOSE trial targets led to clinically meaningful improvements in walking endurance and quality of life, consistent with animal studies that demonstrated that 1000-2000 steps per day are needed to improve hindlimb stepping.[5] Another indicator of attaining a higher dose of exercise was that an average of ~26-27 minutes were spent at >40% HRR during DOSE1 and DOSE2 sessions, compared to a mean of less than 12 minutes during USUAL CARE sessions. [Nonetheless, even 12 minutes of aerobic training per session suggests progress in exercise intensity in stroke rehabilitation in the past 2 decades – in 2002, we reported that people post-stroke spent an average of only 2.8 minutes per physiotherapy session in an aerobic training zone![6]]. Finally, looking to the future, we should take heart about the positive sentiments expressed by both physiotherapists and participants regarding the higher intensity DOSE2 protocol.[7]

STUDY REFERENCE

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