EFFECT OF SUBSYMPTOM THRESHOLD AEROBIC EXERCISE TRAINING IN POST-CONCUSSION SYNDROME: A LITERATURE REVIEW

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ABSTRACT

Background: Concussion is a physiological brain injury that exhibits systemic and cognitive symptoms. The metabolic and physiologic changes of concussion gives rise to altered autonomic function and control of cerebral flow. Aerobic exercise has received increasing importance in the scientific literature as a factor of management for individuals who sustain a concussion. Since exercise training has been reported to lower symptoms and improve function for those experiencing persistent post-concussion symptoms, it presents a potentially useful and clinically pragmatic intervention technique.

Objectives: To monitor and determine if sub symptom threshold exercise preparation is safe and successful for treating post-concussion syndrome.

Methodology: Pub Med, Google scholar, Pedro, Science direct, these databases were searched. Based on PICO format and considering the inclusion and exclusion criteria 6 studies were found eligible for this review. It was observed that sub-symptom threshold aerobic exercise played an important role in improving the PCS symptoms.

Result: A majority of studies show that spontaneous physical activity is safe and that sub-symptom threshold aerobic exercise increases the rate of recovery in post-concussion syndrome. Exercise tolerance can be safely monitored using graded exertion test protocols within days of injury and the extent of early exercise tolerance has diagnostic and prognostic value.

Conclusion: Sub-symptom threshold aerobic exercise is safe and effective for the treatment of Post-concussion syndrome.

Keywords: Post-concussion symptom, Chronic post-concussive symptom, Brain injury, Sub-symptom threshold aerobic exercise.

The World Health Organization defines PCS (Post-Concussion Syndrome) as persistence of 3 or more of the following symptoms after a head injury, such as headache, dizziness, fatigue, irritability, insomnia, concentration difficulty, or has memory difficulty. The majority of patients who are professional players recover from sports- related concussions within 7 to 10 days, while non-athletes recover during the first three months. However, a large number of athletes and non-athletes describe symptoms lasting longer than the time frame specified above, which is referred as post-concussion syndrome.(1)

There's a growing understanding about the personal, medical, societal costs of concussion(2). It is reported that females are at a higher risk of concussion and of developing PCS.(3) Traumatic brain injury and concussion are two of the most common public health issue .Young children have the highest rates of TBI, and men most often as a result of falls and car accidents .Sports –related concussion is also a major public health problem.(2)

Post Concussion Syndrome is a disorder in which the brains regulatory and auto regulatory processes do not naturally revert to normal. Cerebral auto regulation is a term used to describe the ability to maintain a constant perfusion pressure in the face of changing systemic arterial pressure and cerebral blood flow are disturbed following a concussion. Concussion has an effect on not only cognitive performance, but also physiological processes such as the heart and autonomic nervous system. Athletes who have been concussed have exaggerated symptoms. When compared to controls, there has been an increase in the sympathetic nervous activity and heart rates.(1)

While most concussion symptoms disappear within the first month of injury, a significant number of patients continue to have chronic symptoms that last more than a month after the accident, resulting in missed school or work, loss of function and inability to participate in sports.(4) According to the most recent CISG statement from 2016, a brief period of relative rest (24-48) accompanied by a gradual return to activity is now recommended. (5)

Rest, schooling, neurocognitive therapy, and anti-depressants have also been used to treat PCS in the past, with mixed results. Prolonged rest, on the other hand, can cause fatigue, reactive depression, and physiological deconditiong. More athletes and non-athletes are being evaluated and treated for concussions, which is shifting towards an individualized, patient-oriented approach.(2)

Aerobic exercise training can help with concussion –related physiological dysfunction by increasing parasympathetic activity, lowering sympathetic activation, improves blood circulation.(2) Its suggested that by restoring autonomic equilibrium and strengthening cerebral auto regulation, a progressive sub symptom threshold training program would alleviate PCS. Evidence supports sub symptom threshold aerobic exercise as a promising treatment for post-concussion syndrome.(3)

It is often noticed that as a result of caring and funding for a TBI survivor, it takes toll on the physical and mental well-being .They may experience an increased burden of funding the disabled ones by providing physical, financial, and emotional support.(4)

OBJECTIVES: To monitor and determine if sub symptom threshold exercise preparation is safe and successful for treating post-concussion syndrome

METHODOLOGY

SEARCH STRATEGY

✤ KEY WORDS USED:

Medical Subject Heading (MeSH) was used to find relevant keywords. The keywords from other relevant articles were also used. The following keywords were:

Sub symptom threshold aerobic exercises, Post-concussion syndrome, Post-concussion syndrome (MeSH), Post-concussive symptom, Post-concussion symptom, chronic post-concussive syndrome.

✤ DATA BASES SEARCHED

- Pub Med
- ➢ Google scholars
- Science direct

SEARCH TECHNIQUES: Boolean operators "AND" and "OR" were used to search articles.

NO	TERM	NUMBER OF ARTICLES OBTAINED
#1	Sub Symptom Thres Aerobic Exercises	nold 22

#2	"Post-concussion syndrome"; "Post-concussion syndrome"[MeSH]; "Post- concussion symptom"; "Post- concussive symptom"; "Chronic post-concussive syndrome" [search with OR]	2241
#3	#1 AND #2	42

ELIGIBILTY CRITERIA

• INCLUSION CRITERIA

- Articles in English language.
- Articles about Post-Concussion syndrome only.
- International Concussion in Sports Group criteria.
- Fulfill the World Health Organizations International Classification of Disease, Tenth Revision,
 Criteria of symptoms at rest for ≥6 weeks but <52 weeks and demonstrate symptom exacerbation during graded treadmill exercise test.

EXCLUSION CRITERIA

- Articles before 2007.
- Increased cardiac risk.
- A history of moderate or severe traumatic brain injury, defined as a brain injury with an associated Glasgow Coma Scale score of 12 or less.
- Articles whose full text was not received.

DATA EXTRACTION

The articles using different keywords as mentioned above and using different databases accounted for 42 articles. Articles were screened on the basis of three stage approach considering the inclusion exclusion criteria.

- Based on title number of articles obtained: 33
- Based on abstract the number of articles obtained: 18
- Based on inclusion criteria the number of articles obtained:6

So the final number articles for this literature review is 6 which satisfy all the inclusion criteria.



FIGURE1- Flow chart for data extraction.

LITERATURE REVIEW

1.Leddy JJ, et al performed a preliminary study in the year 2010 to evaluate that if the sub symptom threshold exercise training is safe and successful for treating post-concussion syndrome. Twelve refractory patients with PCS out which 6 were athletes and 6 were nonathletes. Five athletes sustained their concussion in sports and 1 in a car accident .Nonathletes sustained their concussion in road traffic accidents or falls at work. The subjects performed an incremental treadmill exercise test according to a standard Balke protocol to the first sign of symptom exacerbation .Blood pressure was measured every 2 minutes, and HR and ratings of perceived exertion by Borg Scale every minute . The subjects were monitored after the termination of the test for 60 minutes. The test was performed before and after 2 to 3 weeks of baseline .Subjects were asked to exercise 5 to 6 days per week at 80% ST heart rate until voluntary peak exertion without symptom exacerbation .Treadmill testing was repeated every 3 weeks. It was observed that after treatment the subjects exercised longer(9.75 \pm 6.38 minutes to 18.67 \pm 2.53 minutes P=.001),and achieved a peak HR (179 \pm 17 bpm) and SBP(156 \pm 13mm Hg) both P< .001,without

symptom exacerbation. Rate of PCS symptom improvement was related to peak exercise HR(r= -0.55,P=.004). Athletes recovered faster as compared to non athletes. Although the mean daily resting symptom reports decreased over time as exercise capability increased, they remained highly variable the degree of variability was present during baseline period too. Thus, daily symptom variability is a part of PCS, with or without exercise When compared to a non treatment baseline, treatment with managed exercise is a healthy regimen that tends to improve PCS symptoms.(1)

2.Baker JG, et al carried out a pilot study in the year 2012 with a vision to provide preliminary detailed information on the functional outcomes(return to physical activity, employment, or other daily activities) of assessment and treatment approach to PCS.Out of 91 patients referred to a university clinic for treatment, a subset of 63 patients were contacted for assessing the symptoms. Those who had symptoms during a graded fitness treadmill test(physiologic PCS,n=40) were compared to those who could exercise to their maximum ability (PCS, n=23).Both groups had been offered progressive exercise rehabilitation. Overall 41 of 57(72%) who participated in the exercise rehabilitation program returned to full daily functioning. This included 27 of 35 (77%) from the physiologic PCS group, and 14 of 22 (64%) from the PCS group. The proportion of patients of patients who returned to their normal functioning was greater compared to the ones who did not exercise. This difference reached significance using Fischer's exact test ,P < 0.002. The descriptive findings of this pilot study show that tracking outcomes, such as return to full daily functioning , is useful for assessing and treating the Post Concussion Syndrome. The small sample size and inclusion of only a subset of participants with follow-up details limit this presentation of pilot studies Participants those without follow-up were those who did not return to the clinic for the same, or those who were unable to reach by phone. Exercise treatment is useful in determining those with physiologic PCS , according to this preliminary descriptive information.(2)

3.Haider MN, et al directed a randomized study in the year 2019 to compare the efficacy of sub symptom threshold aerobic exercise vs. a placebo-like stretching programme for adolescents in the in the acute phase of sport related concussion recovery .A total of 103 participants were allocated (aerobic exercise :n=52;24 female; stretching :n=51;24female) presenting within 10 days of SRC were randomly assigned to aerobic exercise or a placebo-like stretching program regime. Participants of aerobic exercise were instructed to perform aerobic exercise each day on a treadmill under supervision. They were instructed not to stretch before or after aerobic exercise. They were told to rest apart from the prescribed exercise and not to indulge in any other high intensity activity. On the other hand, participants of the stretching group were instructed to follow a prescribed stretching program with same instructions regarding rest. The outcome measure was to determine the days from injury to recovery ;recovery was described as being asymptomatic, having recovery verified by a physician who was blinded. Participants were also classified as having normal(<30 days) or delayed (\geq 30 days)recovery. It was observed that participants in the aerobic group were seen a mean (SD) of 4.9(2.2) days after the SRC, and those in the stretching group were seen a mean (SD) of 4.9(2.4) days after SRC. Participants of the aerobic group recovered in a median of 13 days and

those of the stretching group in 17 days (P=.009 by Mann-Whitney test). There was a non significant lower incidence of delay in the recovery seen in the aerobic exercise group. The research did not look into the mechanism that cause exercise to be effective after a concussion. Participants were not blinded while the ongoing of the treatment which would have led to intervention biasness. This is to our knowledge, that the conducted study shows that prescribing individualized sub symptom threshold aerobic exercise to adolescents with concussion symptoms within the first week after SRC speeds recovery and can minimize symptoms; the likelihood of a prolonged recovery.(5)

4. Chrisman SPD, et al lead a pilot study in the year 2017 to evaluate the safety and possible advantages of the sub symptom threshold exercise program, a rehabilitative intervention for youth with persisting concussion symptoms>1 month. A retrospective chart review of 83 youths out of which 54% females and most had concussion secondary to sports, were conducted who were referred to SSTEP. A sample of patients who had completed at least two SSTEP visits were reviewed and the change in trajectory of symptoms over time were noted before and after initiation of SSTEP. The programme consists of initial evaluation so as to chalk out potential vestibular or cervical spine issues, and then a Balke treadmill test, which gives a heart rate threshold above which the patients report increased symptoms. They must engage in physical activity at the proposed heart rate level for the same amount of time as they were able to sustain physical exercise during the testing(a maximum of 20 minutes). Patients are asked to follow-up in 1-2 weeks and are continued to adhere to the intervention until they complete the Balke treadmill test without causing an exacerbation in the symptoms. Duration of symptoms during the time of presentation were encoded categorically (<6 weeks, 6-12 weeks, >12 weeks) and entered into the model. Mean estimates of SCAT2 overtime were calculated from model adjusted for duration of symptoms. Rate of SCAT2 decrease did not differ significantly by duration of symptoms at presentation(p=0.16). The limitation of this study is that it was a retrospective study where the information about the symptoms prior to the intervention were limited and no control groups. Inspite of the limitations mentioned above, supervised exercise programs appear to be safe and effective for youth. (6)

5.Clausen M, et al supervised a case study in the year 2016. It was observed that some patients who suffered from PCS had reduced exercise capacity, which would be due to a change in the central cardio respiratory regulation. The goal of this study was to verify how well females with PCS controlled their cerebral blood flow during exercise. Nine female athletes with PCS were selected . A reference group of 13 females , non concussed, athletes were recruited. Participants performed a graded exercise test on a treadmill. The participants of both the groups were asked to report on symptom exacerbation/ reached exhaustion. Six of the PCS athletes were subsequently before and after a sub symptom threshold aerobic exercise program . Exercise treadmill test during which BP, minute ventilation, end –tidalCO2, and CBFvelocity were measured. Participants with PCS had lower minute ventilation by 18% and greater end-tidal volume(5%) and CBF(14%) versus the reference group. A significant difference between ($P\leq.05$) between PCS patients post-exercise compared to pre-exercise regime. The limitation

of the above study were inclusion of a reference group as opposed to employing an identical training regimen in healthy subjects . It was therefore viewed that return of normal CBF regulation and exercise tolerance maybe a sign of recovery.(3)

6. Chan C, et al supervised a randomized control study in the year 2018 to examine the tolerability and effectiveness of an active rehabilitation program for adolescents who were slow to retrieve from a sport-related concussion. A secondary aim was to estimate the effectiveness of this intervention. The present study hints a parallel group randomized control trial with blinded assessors. Nineteen adolescents aged 12-18 years with post-concussion symptoms lasting ≥ 1 month after a sports related concussion were enrolled. Treatment as usual consisted of symptoms management and return to play advice and physiatry consultation. The active rehabilitation program involved in-clinic sub-symptom threshold aerobic training along with coordination exercises, and visualization, and imaginary techniques as well as home tailored program over six weeks. The treating physiotherapist recorded in-clinic symptom exacerbation during the rehabilitation. The Post-Concussion Symptom Scale was the primary outcome. A linear mix model with random intercept and fixed effects were fit for groups, time and baseline PCSS score. The effect for group was significant(p=0.047). Nineteen participants were randomized and none dropped. Of the 12 adverse effect (6 in each group), 10 were symptom exacerbation and 2 were emergency department. Inclinic symptom exacerbation occurred in 30% participants but resolved in 24 hours. Active rehabilitation was proved to be effective on Post Concussion Symptom Scale than treatment as usual. The limitation being, the modest sample size may have withheld from identifying rare adverse effects and having enough power to identify small group differences in observed adverse events, The findings recommend active rehabilitation for adolescents with persistent post concussion symptoms in terms of safety, tolerability

RESULTS

Sr.	Title/Author/Year	Sample	Intervention	Duration Intion	Outcome Outc	Outcome Outcom	Result	ulte
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2	Return Violates Full Functioning after Graded Exercise	Exercise Related	Assessment Group 1 Aerobic	S-6days symptom, Intensit Week for old Interve minutes at 80%	Balarice, Aun Philability, exerc Hallig084 exha	Chi-square test ise to Concuss Fishers exact ustion Treadm test	iusefulness no 19 ^f Test.dif	ere was
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Sr. No	Title/Author/Year Of the study	Sample Size	Intervention	Duration Frequency Intensity of the intervention	Outcome	Outcome Measure	Result			
5	Cerebral Blood Flow During Treadmill Exercise Is a Marker of Physiological Post concussion Syndrome in Female Athletes – A Case Study. Clausen M. et al. 2016	N=22	Sub-Symptom Aerobic Treatment Program(Tread mill test)	5-6days per week for 20 minutes at 80% ST heart rate	Blood pressure, Minute Ventilation, End Tidal CO ₂ , CBF velocity.	Post-Concussion Symptom Scale, Trans cranial Doppler , CO ₂ Sensitivity Test.	Sub-Symptom Threshold normalized VE, PETCO ₂ ,CBF and exercise tolerance . CO ₂ Sensitivity and Ventilation improved after exercise treatment.			
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Sr. No	Title/Author/Year Of the Study	Sample Size	Intervention	Duration Frequency Intensity of the intervention	Outcome	Outcome Measure	Result
6	Safety of Active Rehabilitation for persistent symptoms after pediatric sport- related concussion –A Randomized Controlled Trial. Chan C. et al. 2017	N=19 Group 1 (n=9) Group 2 (n=10)	TAU (treatment as usual) and TAU plus active rehabilitation.	6 weeks for 20 minutes.	In- clinic symptoms during aerobic training, Sensitivity to concussion and responsiveness to change associated. Balance, Mood and Cognitive performance.	Post-Concussion Symptom scale. Balance Error Scoring System and Immediate Post Concussion Assessment and Cognitive Test .Beck Depression Inventory scale.	In-clinic symptom exacerbation occurred in 30% of aerobic training sessions, but resolved in 24 hours Therefore Active Rehabilitation was associated with greater reduction on the PCS.
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PEDRO-SCALE TABLE

SR. NO	AUTHOR	PEDR	O SCAL	E	N.						TOTAL SCORE	
		1.	2	3	4	5	6	7	8	9	10	
1	Haider MN. et al	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10
2	Chan C. et al	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10
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DISCUSSION

The main goal of reviewing the literature was to establish the effectiveness of sub-symptom threshold aerobic exercise training in patients with post-concussion syndrome. Sub-symptom threshold aerobic exercise training is useful in treating patients with post-concussion syndrome.

OUTCOME ASSESSED ON THE BASIS OF SUB-SYMPTOM THRESHOLD TRAINING IN POST-CONCUSSION PATIENTS:

PCS symptoms, HR, systolic blood pressure, and rate of recovery were measured as outcomes to determine the effectiveness of sub-symptom threshold exercise in post-concussion syndrome. These were the key outcomes investigated in the six studies mentioned above, five of which found that patients with post-concussion syndrome had inadequate exercise tolerance because their symptoms were aggravated at a critical SBP, At this point, they typically reported an increase in headache/dizziness. After SSTET, subjects reached a peak level of exertion without symptom exacerbation. Subjects reached a high level of exertion after SSTET without experiencing symptom aggravation. Some PCS symptoms are thought to be caused by a disruption in cerebral auto regulation, and that following SSTET, the brain was able to regulate blood flow when the blood pressure rose during exercise. As seen that PCS subjects would show indications of sympathetic nervous system predominance, patients would show evidence of autonomic imbalances which activity would correct by restoring the autonomic balance. However such evidences were not observed because long period of inactivity before study entry and possibility of low volume and intensity of the aerobic training, which was below the threshold required to significantly improve aerobic fitness. The outcome measurements were the sphygmomanometer, Borg scale, and Graded Symptom Checklist. The fact that a few patients exercised to exhaustion without symptom worsening but did not report symptom relief shows that exercise test and symptom reports sense different aspects of PCS. (1) In another article the ability to exercise to maximal capacity without suffering symptoms was examined in the patients who returned , using a structured treadmill procedure devised at the concussion clinic. A bit more than two-third of the population during exercise, symptom aggravation occurred, and these patients were more likely to report headaches and weariness previous to the exercise test. The exercise treatment programme was based on the heart rate at which they experienced symptoms such as irritability, exhaustion, insomnia, headache and Fishers exact test was employed to determine the outcome measure. The results of the follow-up data revealed that almost two-thirds of patients who were referred to clinic for persistent symptoms after concussion returned to daily functioning. It is tough to gauge the consequences on the restoration to full fitness of the exercise rehabilitation programme, since the number of patients who did not participate is small. Some patients are thought to have a permanent physiological disequilibrium and controlled aerobic exercise training may aid in regaining physiological balance. The fact that a patient participated in an exercise rehabilitation programme had no bearing on their ability to return to full daily function. (2) Article suggests that when compared to a placebo-like stretching programme, aerobic exercise improved recovery from SRC in adolescents with concussion symptoms. There was a tendency for aerobic exercise to minimize the delay recovery period. Given the load of socio-economic and academic problems during

prolonged recovery in this age. After the first forty eight hours following SRC, moderate levels of physical activity, including prescribed sub-symptom threshold exercise can safely and dramatically hasten recovery. There were no adverse effects of early sub symptom threshold aerobic exercise, after the first forty eight hours following SRC can safely and significantly speed recovery. Although it showed one near miss. Patients also had access to usual care intervention, such as advice on sleep hygiene, academic accommodations and judicious use of ibuprofen for headache. Buffalo Concussion Treadmill Test. Cognitive evaluation and concussion symptom questionnaire. Mann-Whitney Test. Fisher exact test . Kruskal-Wallis test. Visual Analog scales score were chosen as outcome measures for the study. If early sub threshold exercise has the ability to reduce the need for add on therapies, it could significantly elevate the quality of life. (5) Another article explored that monitored exercise was safe and linked with an exponential trajectory for improvement in concussive symptoms, even in patients who had symptom for more than twelve weeks at initiation of the program. It is unclear whether exercise might help in concussive symptoms, suggestions that experience of symptoms with exercise due to inappropriate cerebral blood flow regulation following brain injury, and that stressing the system by exercising just below the level that causes symptoms may help restore normal cerebral auto regulation. Balke Treadmill Test Symptom portion of the Sport Concussion Assessment Tool, version 2, Akaikes Information Criterion, Bayesian Information Criterion were the outcome measures chosen from the above article.(6) The physiological reaction to arterial CO_2 may be altered by concussion, according to the article. Reduced CO2 sensitivity resulted in a blunted ventilatory response to the increase in VCO2 during exercise. This elevated the PaCO2 that in turn elevated CBF, Sub threshold aerobic exercise treatment normalized the CO2 physiology and exercise capacity of patients with PCS. Progressive step wise aerobic training may improve cerebral auto regulation by conditioning the brain to gradually adapt to repetitive mild elevations of systolic BP. Post-Concussion Symptom Scale, CO₂ Sensitivity Test were the main outcome measures. The response of patients with PCS to exercise treatment is consistent with a normalization of autonomic nervous system function since heart rates during exercise returned to the reference group levels, which has been demonstrated in patients having recovered from moderate to severe traumatic brain injury. In terms of ventilation, a controlled progressive breathing training programme has been proven to improve CO₂ sensitivity. The progressive sub threshold exercise program performed by the patients with PCS may have improved CO_2 sensitivity by stimulating such breathing pattern.(3) Article's main finding was that adverse events were no more common in participants receiving active rehabilitation in addition to TAU compared to those receiving TAU only. A statistically significant treatment effect on post-concussion symptoms was established. It is possible that giving adolescents "permission" to become more active helps to counter maladaptive illness beliefs and encourages them to reinforce into their social and recreational activities. Patients in the active rehabilitation with positive cervical and vestibular exam findings were provided with targeted treatment for these conditions. Post-Concussion symptom scale was the primary outcome measure taken into consideration for the above article. Henceforth all the above mentioned outcomes from respective six articles have proven to be effective in post- concussion syndrome.(7)

FACTORS LIMITING THE EFFECTIVNESS OF SUB-SYMPTOM THRESHOLD THERAPY IN POST-CONCUSSION SYNDROME: Participants who did not get follow-up information were either unable to return to the clinic or could not be reached by phone . There may be discrepancies in the follow-up information in the research undertaken between the groups. The small sample size and descriptive nature of the studies may restrict the inferences that can be made from the results of the statistical comparison and regression analysis. Nonetheless , a rate of return to full functioning at an average of two years after injury of almost three quarters of PCS patients who participated in exercise rehabilitation would appear to indicate the need for further study.(2) Participants may not have been watched during prescribed exercise , and some may have been exercising without the knowledge of the researcher , which would have reduced rather than increased the relative efficacy of aerobic exercise seen. As the participants may not be blinded, intervention bias may occur . They may not have calculated extent of benefit to estimate the potential magnitude of expectancy bias.(5) Despite the fact that difference between the PCS and the reference groups was considerable, because of the probable variability of PCS patients responses, additional research with more individual is needed to confirm these findings.(3)

CONCLUSION

As a result, the preceding studies provide insight into the efficacy of sub-symptom threshold aerobic training in individuals with post-concussion syndrome. PCS patients have a prolonged physiological disequilibrium, and controlled aerobic exercise training can help them regain physiological balance. Control of cerebral blood flow has returned to normal, and exercise tolerance has improved.

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