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Polio Vaccination and Chronic Fatigue Syndrome

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Previous research has suggested that enteroviruses may be implicated in the development and persistence of Chronic Fatigue Syndrome (CFS). One method of investigating this topic has been to use a polio vaccination challenge, and a previous study showed that CFS patients had more shedding than healthy controls. There was no effect of the vaccination on the clinical condition or wellbeing of the CFS patients.
Methods: In the previous study, the control group were more likely to have had a recent booster vaccination. This was controlled in the present study, where 18 CFS patients were randomly assigned to vaccination or placebo conditions. Nine healthy volunteers were also given the polio vaccination.
Results: The results confirmed that vaccination had no negative effects on the CFS group. Although there was more virus shedding in the CFS polio group than in the control polio group, this difference was not significant.
Conclusion: This study confirms that polio vaccination is not contraindicated in CFS patients but could not confirm that they are more susceptible to enterovirus infection.

Keywords: Chronic Fatigue Syndrome (CFS); polio vaccination; enteroviruses; wellbeing; cognition.

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1. INTRODUCTION

There has been considerable research on enteroviruses and Chronic Fatigue Syndrome (CFS). The early studies led to conflicting results [1-3]. Enteroviruses can be broadly categorised into coxsackie viruses A and B, echoviruses, the polioviruses (types 1, 2, 3), and individual enterovirus serotypes. Early descriptions of CFS suggested that it resembled poliomyelitis [4]. Increased neutralising antibodies and IgM antibodies specific to coxsackie B viruses were found in CFS patients compared to healthy controls [5]. Enteroviruses were also more frequent in the faecal samples of those with CFS than controls [3]. This led to the suggestion that CFS may be caused by persistent enteroviral infection [6]. Early results provided mixed support for this view. In one study, CFS patients were found to show more enteroviral persistence in their muscles than healthy controls [7]. However, a later, larger study found no differences between the groups [8]. More recent studies (see [9, 10] for reviews) have also led to conflicting results [11-23].

An alternative approach to CFS and enteroviruses has used the polio vaccine paradigm [24]. This paradigm allows one to examine enterovirus infection after administration of a live booster dose. It has previously been suggested that there is an association between vaccination and CFS [25]. The research examined the possible effects of live poliomyelitis re-vaccination on the symptoms and behaviour of CFS patients and healthy controls. In addition, differences in the two groups immune responses to the vaccine challenge were also investigated. Vaccination did not change the clinical condition of the CFS patients, and their T- and B-cell polio-specific responses were no different from the healthy volunteers. However, the CFS patients did shed higher poliovirus levels, as identified by direct isolation, compared to the healthy controls. This study showed that live poliovirus vaccination in CFS patients is not contraindicated, which argues against the view that CFS is exacerbated by vaccinations. In addition, it is unlikely that a specific immune defect in response to enteroviruses can account for the pathogenesis of CFS. However, the increased poliovirus shedding in the CFS patients requires further study, and the underlying mechanisms still need to be identified.

Many of the findings linking enteroviruses to CFS have been criticised in terms of poor methodology. In the original polio vaccine study, the control group had been given “booster” vaccinations more recently than the patients, which could plausibly account for the increased virus shedding. The present study addressed this by using a healthy control group that was matched with the CFS group in terms of the timing of the primary polio vaccination. The aims of the study were identical to the original one, namely, to determine whether polio vaccination of CFS patients led to any adverse effects and to examine virus shedding after vaccination.

2. METHODS

The study was approved by the local, regional ethical committee and carried out with the informed consent of the participants.

2.1 Participants

Eighteen patients with CFS, diagnosed according to the Oxford criteria, were recruited randomly from a panel of those who had in the past or were currently attending the University of Wales College of Medicine (UWCM) CFS outpatient clinic. The demographic characteristics and illness history of these patients can be shown in Tables 1 and 2. In general, the profile of this sample was consistent with those of the typical patients attending the clinic from which they were recruited and of other CFS populations reported in the literature. A further nine individuals without CFS were recruited from the partners of the CFS patients taking part.

2.2 Study Design

Eighteen patients with CFS and nine individuals without CFS were recruited into a 28-day double-blind study to determine any effects of poliovirus vaccination in individuals with CFS. On day 0, the healthy controls received the poliomyelitis vaccine (SmithKline Beecham), a live (Sabin) polio vaccine containing a mix of attenuated poliovirus types 1,2 and 3 (6 log10 poliovirus 1, 5 log10 poliovirus 2 and 5.5 log10 poliovirus 3) while the patients with CFS were randomly allocated into either the placebo (sterile saline) or vaccine treatment groups and both the patients and experimenters who conducted the investigation were blind to which individuals received the vaccine. All individuals were followed up on four occasions thereafter (days 2, 7, 14, 28 post-vaccination).

Table 1. Demographic characteristics of CFS patients and controls

	CFS patients (vaccine)	CFS patients (placebo)	Controls (vaccine)
Sex (%)	57 Female 43 Male	75 Female 25 Male	25 Female 75 Male
Age Range	38 – 65 years	46 – 54 years	39 – 65 years
Marital status (%)			
Single	14	-	25
Married	86	100	75
Education level (%)			
Primary education only	7	-	-
Left school before 16	36	25	38
Completed 'O' levels	29	25	12
Completed 'A' levels	-	25	12
At least one year at the	-	25	12
University	21	-	12
BSc or BA PhD, MD or other	7	-	12

Table 2. Clinical profile of the CFS patients and controls

	CFS patients (vaccine)	CFS patients (placebo)	Controls (vaccine)
Mean duration of illness (months)	126.3	107.5	N/A
Mean time since diagnosis (months)	73.8	52.0	N/A
Current severity (%)			
Worse than at any stage	14	0	N/A
Bad	14	50	
Bad with some recovery	43	50	
Recovering with relapses	29	0	
Completely recovered	0	0	
Symptoms (%) – at time of study			
Physical weakness (Yes)	79	100	37
Excessive fatigue	93	100	25
Legs feeling heavy	79	75	25
Muscle pain	71	100	-
Pain in chest	43	25	-
Painful joints	79	100	12
Nausea	29	25	-
Indigestion	43	50	12
Bloated stomach	50	75	12
Wind	57	50	25
Sore throat	57	50	-
Headache	57	50	12
Earache	36	50	-
Sore eyes	50	50	12
Sensitive to noise	71	75	-
Sensitive to light	64	100	12
Feeling hot/cold	86	75	12
Sweating	71	75	-
Shivering	43	50	-
Swollen glands	79	50	-
Racing heart	43	75	-
Insomnia	36	100	12
Depression	50	75	25
Anxiety	57	50	-
Loss of concentration	79	100	-
Loss of memory	79	75	25
Allergies	29	0	-

2.3 Virology

Pan-enterovirus and poliovirus-specific assays were developed and utilised for this part of the study. A method based on nucleic acid sequence-based amplification (NASBA) was found to be suitable for the analysis of poliovirus shedding [26]. NASBA has been found to be a suitable alternative to RT-PCR for the detection of enterovirus sequences. These kit-based reagents have enabled a wide range of laboratories to use molecular-based diagnostic procedures to identify RNA viruses.

2.4 Clinical Assessment

Subjective and objective assessments of the physical wellbeing of the sample were undertaken throughout the investigation by:

- completion of a physical symptoms index at the start and a questionnaire completed at week 0 and week 4 of the study, which examined fatigue-related and somatic symptoms.
- The objective assessments were undertaken by the clinician responsible for the CFS patient group, who arranged a consultation session for each patient on days 0 and 28. The clinician was blind to the treatment group into which each patient had been allocated.

2.5 Psychosocial Assessment

A series of questionnaires were administered to examine demographic and illness characteristics, current symptoms, and psychosocial measures. The second series of questionnaires were administered during the study: these examined: symptoms [24], mood [27], depression [28], state anxiety [29], emotional difficulties, cognitive difficulties, somatic symptoms, and fatigue [30].

2.6 Cognitive Assessment

Subjective ratings of cognitive function [31] and objective assessments of cognitive functioning (simple reaction time and cognitive vigilance [32]) were undertaken during the study.

3. RESULTS

3.1 Virus Shedding Results

Table 3 shows the virus shedding on days 2, 7, 14 and 28 in the controls and the CFS vaccine and placebo groups. More patients than controls shed virus following vaccine challenge, but this effect was not significant.

3.2 Effects of Vaccination on Mood, Symptoms, and Performance

Table 4 shows the wellbeing scores for the controls and CFS vaccine and CFS placebo groups. There were no significant effects of vaccine challenge on subjective reports of health and wellbeing.

Table 5 shows the cognitive performance scores for the controls and CFS groups. The CFS groups were slower and less accurate than the controls, but there were no effects of vaccination in the CFS sample.

4. DISCUSSION

The present study was part of a larger programme on viral infections and CFS. Previous research has attempted to demonstrate a role for enteroviruses in the aetiology and pathogenesis of CFS. These studies have led to inconclusive results. However, there is evidence that CFS patients may be more susceptible to viral infections. In the first part of our research, prospective studies of upper respiratory tract illnesses (URTIs) were conducted [33, 34]. The results showed that CFS patients reported more URTIs, and the virology showed a greater number of infections confirming that the difference between the CFS and healthy groups was not due to a reporting bias. Indeed, similar virus identification rates were obtained in patient and control groups with clinical illnesses suggesting that identical mechanisms were in operation but that the CFS patients had more infections and illnesses. The results also showed that the CFS patients had more sub-clinical infections, which again supports the view that this group are particularly susceptible to acute infections.

The present study was unable to replicate our previously reported finding that CFS patients are more likely to shed virus following polio vaccine challenge [24]. In the original study, the control group had been given “booster” vaccinations more recently than the patients, which plausibly accounts for our earlier results. The study did confirm that vaccination had no detrimental effect on the patients, which supports our earlier view that it is unlikely to cause the type of problem suggested by some sources.

Table 3. Poliovirus shedding in patients and controls

	Controls	CFS Vaccine	CFS Placebo
Day 2 (%)	12	21	0
Day 7	37	36	0
Day 14	12	21	0
Day 28	12	14	0

Table 4. Baseline and post-vaccination questionnaire scores (means, s.d.s in parentheses)

	Controls		CFS Vaccine		CFS placebo	
	Day 0	Day 28	Day 0	Day 28	Day 0	Day 28
Positive Mood (2)	38.62 (7.07)	38.87 (7.36)	31.07 (9.18)	28.46 (7.79)	31.75 (11.73)	33.33 (2.31)
Negative Mood (1)	8.50 (5.48)	6.62 (4.21)	20.71 (9.53)	21.16 (6.59)	18.50 (8.70)	17.67 (11.93)
Centre for Epidemiologic Studies Depression Scale (1)	27.12 (8.04)	28.12 (8.13)	37.50 (9.29)	38.69 (9.02)	35.00 (9.56)	35.00 (9.54)
State Anxiety (1)	29.50 (6.19)	32.75 (6.63)	39.93 (9.92)	42.31 (12.82)	34.75 (7.89)	37.00 (6.56)
Emotional Distress (1)	20.50 (5.01)	22.00 (7.13)	45.28 (22.88)	42.08 (15.06)	35.00 (19.34)	31.00 (19.47)
Fatigue (1)	25.12 (17.87)	21.62 (12.18)	60.28 (15.39)	62.38 (12.93)	61.75 (11.95)	48.67 (4.16)
Cognitive Difficulty (1)	17.12 (11.44)	15.50 (4.69)	48.43 (16.46)	48.31 (14.53)	40.25 (17.82)	38.00 (17.00)
Somatic Stress (1)	19.87 (3.27)	20.12 (4.26)	55.93 (21.93)	57.23 (19.53)	53.25 (30.43)	53.00 (19.31)
Beck Depression Inventory (1)	5.37 (4.66)	5.25 (4.65)	12.86 (6.61)	13.08 (5.56)	11.25 (9.21)	8.33 (3.78)

(1) High scores = greater impairment ; (2) Low scores = greater impairment

Table 5. Baseline and post-vaccine scores for the performance tests (means and s.d.s)

	Controls		CFS Vaccine		CFS Placebo	
	Day 0	Day 28	Day 0	Day 28	Day 0	Day 28
SRT – mean RT msec	359.62	321.12	383.57	411.69	480.50	488.00
Repeated digits vigilance task – Mean Hits	14.13	16.50	12.57	11.31	12.50	13.67

5. CONCLUSION

Previous research has suggested that enteroviruses may be involved in the aetiology and pathogenesis of CFS. One method has used a polio vaccine challenge to examine possible differences in CFS patients ability to deal with viruses. An initial study showed no negative side effects of the polio vaccine but did demonstrate greater virus shedding in the CFS group. The present study confirmed that polio vaccination leads to no negative outcomes in the CFS group. However, it could not replicate the greater virus shedding in CFS patients after polio vaccination.

CONSENT

The research was carried out with the informed consent of the participants.

ETHICAL APPROVAL

The research was carried out with the approval of the local regional ethics committee.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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