CORRESPONDENCE

# Re-evaluation of the relationship between migraine and persistent foramen ovale and other right-to-left shunts

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Right-to-left shunts (usually persistent foramen ovale) are responsible for a large proportion of cases of decompression illness [1,2]. Previously, we reported in *Clinical Science* [3] a review of the medical records of 200 consecutive individuals investigated for the cause of their decompression illness that showed that those with a large right-to-left shunt had a considerably increased prevalence of migraine with aura in daily life unconnected with diving, but not of migraine without aura. They also had an increased incidence of migraine aura after dives that liberate venous bubbles [3]. Transcatheter closure of persistent foramen ovale and atrial septal defects usually reduces the severity and frequency of attacks of migraine with aura [4]. Atrial shunts are dominantly inherited and this inheritance is closely associated with the inheritance of familial migraine with aura [5]. However, a significant role for right-to-left shunts in migraine aetiology does not accord with the generally accepted theories that migraine is a primary disorder of the brain [6]. Accordingly, we re-evaluated the observations reported previously in *Clinical Science* [3] in a further consecutive series.

Data was collected from the next 200 consecutive divers (61 female) who attended our special clinic for investigation of decompression illness after the series we reported previously [3]. As part of clinical assessment, the history and the results of contrast echocardiography were recorded. Methods were identical with those reported previously [3]. In brief, we asked about migraine symptoms defined according to the International Headache Society both in daily life (unconnected with diving) and after dives [7]. Transthoracic contrast echocardiography was used to detect the presence of a right-to-left shunt and for semi-quantitative assessment of the shunt size as described previously [3]. Statistical analysis of categorical variables was with the $\chi^2$ test. Yates's correction was used for 4-fold tables. A value of $P < 0.05$ was considered to be significant. The Shropshire Research Ethics Committee approved the study.

A total of 119 (59.5 %) of the 200 divers with a history of decompression illness reported in the present study had a shunt compared with 120 of 200 (60 %) in the previous study ([3]; see Table 1). From inspection of Table 1, it is clear that the findings in the present study are very similar to those in the study we performed previously [3]. Large right-to-left shunts, and particularly large shunts at rest, are found frequently in divers who have had decompression illness.

As previously, there was no significant difference in prevalence of migraine without aura in daily life between cases grouped according to the presence and size of shunts. Migraine with aura (or episodes of migraine aura without headache) that occurred at times unconnected with diving was reported by 67 (33.5 %) of the 200 divers in the present study compared with 26.5 % in the previous study [3] (the difference was not significant). All individuals with migraine aura experienced fortification spectra, but seven divers (five with a large shunt at rest, one with a large shunt with a Valsalva manoeuvre and one with no shunt) also had hemimotor and/or hemisensory symptoms/signs. In the previous study [3], ten divers had hemiplegic migraine and eight of them had large shunts at rest. As in the previous study [3], migraine with aura unconnected with diving was significantly ($P < 0.001$) more frequent in those with a large shunt that was present at rest (52 out of 90; 57.8 %) than in other groups without or with a shunt (15 out of 110; 13.6 %).

A total of 32 divers in the present study compared with 27 in the previous study [3] described migraine aura without or with headache after surfacing from a dive. This symptom was predominantly associated with the presence of a large shunt and a dive profile that would have liberated venous bubbles. The aura consisted of fortification spectra in all cases. In addition, hemimotor or hemisensory symptoms occurred after diving in five divers in the present study, each of whom had a large shunt, compared with nine divers in the previous

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**Table 1 Relationship between migraine and right-to-left shunts**

Data from the previous study [3] are shown in parentheses.

| | Migraine not connected with diving | | | |
|---|---|---|---|---|
| | Without aura | With aura | Migraine aura after diving | Total |
| No shunt | 5 (7) | 8 (11) | 2 (1) | 81 (80) |
| Small shunts | | | | |
| At rest | 1 (0) | 0 (1) | 0 (1) | 2 (8) |
| With Valsalva | 0 (2) | 0 (0) | 0 (0) | 4 (10) |
| Total | 1 (2) | 0 (1) | 0 (1) | 6 (18) |
| Medium shunts | | | | |
| At rest | 0 (0) | 2 (1) | 1 (1) | 4 (5) |
| With Valsalva | 0 (0) | 0 (0) | 0 (0) | 2 (1) |
| Total | 0 (0) | 2 (1) | 1 (1) | 6 (6) |
| Large shunts | | | | |
| At rest | 3 (6) | 52 (38) | 25 (21) | 90 (80) |
| With Valsalva | 0 (3) | 5 (2) | 4 (3) | 17 (16) |
| Total | 3 (9) | 57 (40) | 29 (24) | 107 (96) |
| Column totals | 9 (18) | 67 (53) | 32 (27) | 200 (200) |

study [3]. Two of the divers in the present study had more than eight episodes of hemiplegic migraine after surfacing from dives and one of these also had hemiplegic migraine after contrast echocardiography.

In this re-evaluation of the relationship between migraine and right-to-left shunts, the findings were very similar to those in our previous study [3]. These data confirm the observation that migraine with aura, but not migraine without aura, is much more frequent in individuals who have a right-to-left shunt than in those with no shunt [3,8,9].

Our data also show that there is a relationship between shunt size and prevalence of migraine with aura. Migraine with aura was 4.5 times more prevalent in those with a large shunt present at rest than in those with no shunt (52.9 % compared with 11.8 %). Individuals with a small shunt (at rest or with a Valsalva manoeuvre) have a lower prevalence of migraine with aura, similar to those with no shunt. Individuals with a medium shunt at rest or a large shunt with a Valsalva manoeuvre have an intermediate prevalence of migraine with aura.

Slight differences between our findings and those of Del Sette et al. [8] and Anzola et al. [9] are probably because their techniques for detecting right-to-left shunts may have missed small shunts, as indicated by rates for prevalence of shunts in their control populations of 16 and 20 % respectively [8,9]. These are lower than the 27.3 % prevalence reported in a large post-mortem study [10], which is very similar to the 27.6 % found in our control group [1].

In both the present study and the previous study [3], we observed that individuals who had auras after diving usually have a large shunt. These data show that individuals with a history of migraine with aura are at increased risk of decompression illness, because both conditions are facilitated by the presence of a large right-to-left shunt. Accordingly, individuals with a history of migraine with aura should be screened for the presence of a large shunt before they dive or are exposed to subatmospheric decompression.

This re-evaluation confirms our previous observations [3]. It supports our hypothesis that the lungs may have a role in filtering substances in the venous blood that trigger migraine with aura and that passage of blood through a right-to-left shunt may facilitate attacks of migraine by circumventing the lung filter. A properly designed interventional study is required to test this hypothesis.

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