Pflügers Arch. 356, 159–167 (1975)

Comparison of Cisternal and Lumbar Cerebrospinal Fluid pH in High Altitude Natives

M. C. Blayo, J. Coudert, and J. J. Pocidalo

Unité de Recherches de Réanimation—U 13 I.N.S.E.R.M.

Hôpital Claude Bernard, Paris, France and

Instituto Boliviano de Biología de la Altura-Facultad de Medicina, La Paz, Bolivia

Received February 3, 1975

Summary. Samples of cisternal or lumbar cerebrospinal fluid were obtained from 20 young male volunteers born and living at high altitude (3500 to 4800 m). The pH, carbon dioxide and oxygen tensions, and bicarbonate concentration were measured and compared with those in the arterial and jugular venous blood.

A consistent difference between the two CSF compartments was noted, particularly a lower pH (0.05), a higher P_{CO_2} (7 Torr), and a lower P_{O_2} (7 Torr) at the lumbar site. Mean bicarbonate concentration was not significantly different at the two sites. The main factor is P_{CO_2}, which controls the pH variation.

These differences were more marked in high-altitude natives than in man at sea level.

The existence of a consistent inhomogeneity of CSF acid-base content emphasizes the inaccuracy of using lumbar CSF pH to estimate the ECF pH as regulator of pulmonary ventilation and determinant of cerebral blood flow.

Key-words: Acid-Base Balance — Oxygen Partial Pressure — Cerebrospinal Fluid — High Altitude.

Over the past few years investigators have shown an increasing interest in cerebrospinal fluid (CSF)pH regulation since the pH value of the extracellular cerebral fluid (ECF) is thought to be the regulating factor of both pulmonary ventilation [14] and cerebral blood flow [6,18].

High-altitude natives have a particular acid-base balance associated with chronic hypoxia and hypocapnia. The study of CSF pH seemed best suited to understand the ventilatory regulation resulting in this chronic state of hypocapnia. According to Sørensen *et al.* [21], CSF pH is lower in high-landers than in low-landers and may explain the hyperventilation in high-altitude natives who lack hypoxic drive from the peripheral chemoreceptors [21,22]. However, other investigators have found CSF pH values within the normal sea-level range [19,10].

We recently showed that cisternal CSF pH is much higher than has been reported by others and suggested that these differences were related to the CSF sampling site [2]. The aim of the present work was to test this hypothesis by comparing the acid-base status and P_{O_2} of both lumbar and cisternal fluid in natives from La Paz (3800 m) in the Andes. We found consistent discrepancies between lumbar and cisternal acid-base status in man born and living at high altitude and concluded that lumbar CSF cannot be considered to be the same as cerebral CSF.

Material and Methods

a) *Subjects and Experimental Protocol.* Twenty young, adult men, all volunteers, were studied. They were either pure Indian or crossbred (Quechua or Aymara) who were born and had always lived at a high altitude.

In 9 of them (group C) samples of cisternal CSF, arterial blood, and blood from the internal jugular vein were collected according to a method previously described [2].

In the remaining 11 (group L) the lumbar CSF was obtained as follows: the subjects were placed in supine position and samples of blood from the femoral artery and the internal jugular vein were collected simultaneous. Within the following 5 min a sample of lumbar CSF was withdrawn from the L_5-S_1 or the L_4-L_5 space. Thereafter the subjects were asked to stay in prone position for 2 hrs, then in supine position, they were kept under medical supervision for 24 hrs.

CSF and blood samples were withdrawn anaerobically and analyzed immediately.

b) *Measurements.* pH was determined using a capillary glass electrode with a calomel reference electrode (Radiometer type E 5021), both maintained at 37°C. The electrode was calibrated with two NBS buffer solutions of pH 7.384 and 6.840, respectively, at 37°C. The recommendations of Leusen and Van Heijst *et al.* were applied for CSF pH measurements [11,23].

P_{CO_2} was measured directly with a Gleichmann and Lübbers electrode [9] calibrated daily with 3 gas mixtures of various CO_2 concentrations previously determined by the Scholander micro-method.

These gas mixtures were humidified and heated to 37°C before use. For any given P_{CO_2}, the electrode response was identical in the gaseous phase, in the blood, and in the CSF.

P_{O_2} was measured directly by a polarographic method using a platinum macro-electrode fitted with a magnetic stirring system [9]. For reliable measurements of CSF P_{O_2} stirring is necessary [8]. The electrode was calibrated with 3 different gas mixtures and pure N_2. Measurements in blood equilibrated at a known P_{O_2} enabled us to evaluate the difference between blood and gas readings; no such difference existed between the equilibrated CSF and the gaseous phase.

The pH, P_{CO_2}, and P_{O_2} electrodes were connected to a combi-analyzer U.D. (L. Eschweiller U.C., Kiel).

$[HCO_3^-]$ was calculated from the Henderson-Hasselbach equation using the pH and the P_{CO_2} values and taking the CO_2 solubility constants at 37°C as 0.0308 and 0.0318 $mM \cdot l^{-1} \cdot torr^{-1}$ for plasma and CSF, respectively, and the generally accepted value for pK′ (Severinghaus *et al.* [20] Mitchell *et al.* [13]).

c) *Statistical Analysis.* In each group, the means and the deviations of each variable were determined. For all variables within a group, differences between blood and CSF were tested by the method of pairs. Differences between the two groups were determined by comparison of the two means and using the *t*-test, P values being read from the Student-Fisher table.

Results

The data are given in Table 1.

The arterial blood acid-base balance of the two groups was similar; no difference could be found between pH and P_{CO_2} values, nor between HCO_3^- concentrations. But a significant difference existed between the P_{O_2} values ($P < 0.05$), Pa_{O_2} being 2.8 Torr higher in group L than in group C.

Slight differences between the pH and the P_{O_2} of the two groups were evidenced in the cerebral venous blood, but they might be attributable to the site of sampling; this will be discussed below. Thus blood acid-base status was practically identical in both groups.

Cisternal CSF pH was significantly ($P < 0.001$) higher than lumbar CSF (a mean of 0.05 unit). All individual values of arterial and CSF pH are plotted in Fig. 1; the difference between arterial and CSF pH values was larger in group L (0.097) than in group C (0.047). These differences were significant ($P < 0.001$) in either group. Moreover, the magnitude of the discrepancies differed significantly ($P < 0.001$) from one group to the other.

The cisternal P_{CO_2} was significantly lower than the lumbar P_{CO_2} by approximately 7 Torr. Differences between arterial and CSF P_{CO_2} values were highly significant ($P < 0.001$) and the difference between the magnitudes of each group was significant ($P < 0.01$).

No significant differences could be found between cisternal and lumbar CSF $[HCO_3^-]$.

Table 1. Acid-base balance and P_{O_2} in cisternal and lumbar CSF and in arterial blood and internal jugular venous blood of high-altitude natives

		pH	P_{CO_2} Torr	$[HCO_3^-]$ mEq. l^{-1}	P_{O_2} Torr
CSF	cisternal (gr. C)[a]	7.366 ± 0.024***	37.3 ± 2.3***	20.5 ± 2.0	32.0 ± 2.3***
	lumbar (gr. L)[b]	7.317 ± 0.019	44.0 ± 2.8	21.4 ± 1.2	25.0 ± 1.6
a	gr. C	7.413 ± 0.024	31.0 ± 1.5	20.0 ± 1.6	56.6 ± 2.9*
	gr. L	7.414 ± 0.017	32.7 ± 2.1	21.1 ± 1.2	59.4 ± 2.8
v	gr. C	7.349 ± 0.029*	41.8 ± 2.6	23.2 ± 2.0	28.0 ± 1.9*
	gr. L	7.370 ± 0.014	41.1 ± 2.0	23.9 ± 1.1	32.1 ± 4.6

The data are the mean values of the measurements ± standard deviation.
[a] gr. C: Group of 9 subjects whose cisternal CSF was studied.
[b] gr. L.: Group of 11 subjects whose lumbar CSF was studied.
* Significant difference ($P < 0.05$) between gr. C and gr. L.
*** Significant difference ($P < 0.001$) between gr. C and gr. L.

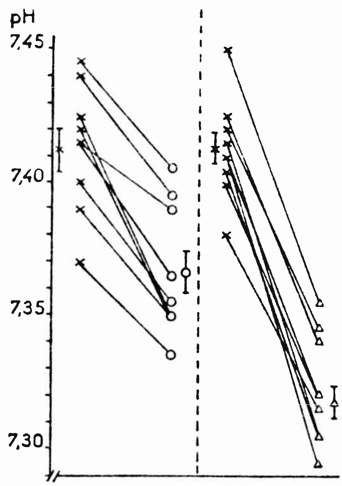

Fig. 1. pH of arterial blood and of cisternal and lumbar CSF in high-altitude natives symbols: × arterial blood; ○ cisternal CSF; △ lumbar CSF. The mean values for each fluid of either group are given; bars indicate ± standard error of the mean

P_{C2} of cisternal CSF was 7 Torr higher than that of lumbar CSF ($P < 0.001$). The differences of 24.7 Torr between arterial and CSF P_{O_2} in group C and 34.4 Torr in group L were highly significant ($P < 0.001$).

Discussion

First we shall justify the comparison of two groups of different subjects and compare the present data with those obtained from natives either at high altitudes or at sea level. Then the acid-base balance difference between cisternal and lumbar CSF, and the magnitude of the difference between data collected at high altitude and at sea level will be discussed.

1. The comparison of lumbar and cisternal CSF acid-base status would be more accurate if samples of both fluids had been withdrawn simultaneously in the same subjects. But owing to the technical difficulty of such a protocol, the study had to be performed in two groups of different subjects with reference to their blood acid-base status.

The arterial acid-base balances of the two groups were found to be similar but for a slight difference in the Pa_{O_2} values, the averages of which were 56.6 Torr in group C (9 men) and 59.4 Torr in group L (11 men). They were remarkably close to each other, as well as to those reported elsewhere in natives at the same altitude: 57.0 Torr in the study of Severinghaus *et al.* [19] and 57.1 Torr in the work of Cudkowicz *et al.* [4]. In each group the difference between the arterial P_{O_2} values varied in a direction opposite to that of CSF, since CSF P_{O_2} is higher in group C.

Likewise, only slight discrepancies were found between the internal jugular blood data of the two groups that might be explained by the difference in site; in group C venous blood was collected above the jugular sinus while in group L it was obtained from the internal jugular vein. In addition the jugular venous blood pH and P_{O_2} differences between the two groups were opposite those of CSF.

Therefore, we concluded that the blood acid-base balances of both groups were similar and felt justified in comparing the cisternal and the lumbar CSF acid-base values.

2. The comparison of lumbar and cisternal CSF in high-altitude natives confirms a previous hypothesis following which the CSF acid-base balance varies according to the sampling site [2].

Lumbar CSF pH had a mean value of 7.317, almost the same as that reported by other investigators in high-altitude natives: 7.327 by Severinghaus *et al.* [19] and 7.328 by Lahiri *et al.* [10], but different from Sorensen's data who found a CSF acidosis (7.295) with a strictly normal arterial pH [22]. In addition, the pH of lumbar CSF appeared "normal" when compared with data from control sea-level subjects: 7.325 by Van Heijst *et al.* [23], 7.331 by Gänshirt [7], 7.329 by Blayo *et al.* [1]. The same was true for the arterial blood pH.

Cisternal CSF pH was markedly more alkaline: 7.366 in group C. No data could be found in the literature on high-landers' cisternal CSF acid-base balance. But Van Heijst *et al.* [23], Gänshirt [7], and Plum *et al.* [15] found that the pH of cisternal CSF was significantly higher than the lumbar CSF at sea level.

Lumbar CSF P_{CO_2} (44.0 Torr) was similar to that reported by Severinghaus *et al.* (43.2), and Sorensen *et al.*: 46.0 Torr [19,21]; it reached higher values than the internal jugular vein P_{CO_2} (41.1 Torr).

Cisternal CSF P_{CO_2} (37.3 Torr) was significantly lower than lumbar CSF and was between the arterial P_{CO_2} (31.0 Torr) and the cerebral venous P_{CO_2} (41.8 Torr). The present results differ from reports in which lumbar and cisternal pH and P_{CO_2} were similar and lumbar P_{CO_2} was equal to cerebral venous blood [3,5]. Thus it did not seem feasible, as suggested by Pappenheimer *et al.*, to calculate the CSF pH from CSF $[HCO_3^-]$ and cerebral venous blood P_{CO_2} [14]. On the other hand, the value found for cisternal CSF P_{CO_2} was consistent with that predicted according to Ponten *et al.* [16]: it was almost equal to the arithmetic mean of Pa_{CO_2} and Pv_{CO_2}. This relationship was confirmed in high-altitudes natives.

Lumbar CSF $[HCO_3^-]$ did not differ from cisternal CSF, as was also found at sea level [23]. Thus the pH difference between lumbar and cisternal CSF might be due only to P_{CO_2} difference.

Lumbar CSF P_{O_2} (25.0 Torr) was well below cisternal CSF P_{O_2} (32.0 Torr). The only values of lumbar P_{O_2} found in the literature [22] were from 4 subjects with "chronic mountain polycythemia", whose acid-base balance and arterial P_{O_2} differed much from normal highlanders and could not be compared to ours. Nevertheless, lumbar CSF P_{O_2} in high-altitude natives is lower than in natives at sea level [1,7].

We have no data on cisternal CSF P_{O_2} at sea level, but Gänshirt [7] demonstrated an important difference between lumbar and cisternal P_{O_2}. Cisternal P_{O_2} was 10 Torr higher than lumbar, P_{O_2} in 15 subjects from whom simultaneous samples of lumbar and cisternal CSF were taken, while cisternal P_{O_2} from 64 normal subjects and lumbar P_{O_2} from 117 other subjects had a mean difference of 9 Torr. In addition, the mean lumbar P_{O_2} reported by Gänshirt was 6 Torr higher than ours at sea level. This could be explained by differences in methods: Gänshirt used vaseline-rinsed glass syringes and micro-electrodes. Both might be responsible for higher P_{O_2} values in fluids with small O_2 contents, since O_2 is soluble in oil and air contamination are more likely when micro-electrodes including capillary tubes are used. Yet P_{O_2} differences (9 to 10 Torr) between cisternal and lumbar fluids evidenced by this author in subjects at sea level are close to those documented here at a high altitude (7 Torr), the difference between them probably being due to the oxygen level.

Thus a difference does exist between lumbar and cisternal CSF acid-base balances in high-altitude natives; lumbar P_{CO_2} is higher, resulting in a more acid pH and a lower P_{O_2} than in cisternal fluid.

3. Van Heijst [23] and Gänshirt [7] demonstrated discrepancies between the acid-base values of lumbar and cisternal CSF at sea level. A comparison of their findings with ours at a high altitude is presented in Table 2.

First, it was evident that Van Heijst's and Gänshirt's results differed especially with regard to P_{CO_2} values. The comparative study of the acid-base status in cisternal and lumbar fluid documented by Gänshirt lacks arterial blood data. Elsewhere in the same paper, but in another group of 14 subjects, the mean cisternal P_{CO_2} was 39.3 Torr, and the arterial blood P_{CO_2} was 30.6. In the first group, of interest here, the mean cisternal P_{CO_2} was 36.8 Torr; therefore the arterial P_{CO_2} would be below 30 Torr. Such a P_{CO_2} cannot be considered normal whatever the reasons are, owing to the method (as discussed above) or to the subjects being in pathological or unsteady-states as suggested by the dispersion of measurements. This low P_{CO_2} is responsible for unusually low bicarbonate concentrations.

Therefore the differences between lumbar and cisternal CSF acid-base values encountered in high-altitude natives can be compared only to

Table 2. Comparison of acid-base balance in cisternal and lumbar CSF between sea level (Van Heijst et al. [23] and Gänshirt [7] and high-altitude natives (present data)

		pH	P_{CO_2}	$[HCO_3^-]$	P_{O_2}
High altitude	C	7.366	37.3	20.5	32.0
(present data)		0.024	2.3	2.0	2.3
	L	7.317	44.0	21.4	25.0
		0.019	2.8	1.2	1.6
Sea level	C	7.346	46.5	24.7	
(Van Heijst)		0.021	1.9	1.1	
	L	7.325	49.1	24.9	
		0.024	2.2	0.8	
Sea level	C	7.361	36.8	20.0[a]	47.1
(Gänshirt)		0.033	6.7	3.6	4.5
	L	7.331	44.4	22.3[a]	36.8
		0.035	7.4	3.4	6.1

The data are the mean values of the measurements ± standard deviation. C: cisternal cerebrospinal fluid; L: lumbar cerebrospinal fluid.

[a] The bicarbonate values were calculated using Gänshirt's P_{CO_2} and pH meas-surements

Van Heijst's data whose 13 subjects had a strictly normal arterial acid-base balance. The pH discrepancy was greater (0.049) at a high altitude than at sea level (0.021). But both the former and the latter agreed with the P_{CO_2} differences: 6.7 Torr at a high altitude, 2.6 Torr at sea level; CO_2 levels differed between altitude and sea level. Although $[HCO_3^-]$ was markedly lower in high-altitude natives, its differences between lumbar and cisternal CSF were neither significant at altitude nor at sea level.

4. The most probable explanation for the difference in oxygen and carbon dioxide tensions between cisterna magna and lumbar sac spinal fluid is based on regional differences in tissue. The respiratory gases are readily diffusible within the cerebrospinal fluid; their partial pressure reflects tonometrically the mean tension in the adjacent tissues and their respective regional blood vessels. It is evident that the cisterna magna and the lumbar sac being far apart are surrounded by different tissues with different superficial vascularization [15]. The cisternal lumbar difference in acid-base status and P_{O_2} tension reflects discrepancies in the ratio of local metabolism to blood flow in these areas.

The magnitude of the difference between cisternal and lumbar CSF, at altitude and at sea level, is in all likelihood attributable to the hemodynamic changes in the brain at altitude. It has been shown before that hypocapnia due to high altitude results in a decrease of cerebral blood flow, and we showed recently that a fall in the rate of blood flow is accompanied by a rise in the arterio-venous difference in oxygen [2]. Therefore arterio-venous difference in CO_2 must be increased as well, resulting in a higher venous P_{CO_2}.

In conclusion, these results, demonstrating that the acid-base status and P_{O_2} of cisternal CSF are different from lumbar CSF in high-altitude natives, are consistent with those obtained at sea level in normal people [23] and in acutely ill patients [15]. In addition, the fluid in the choroid plexus has a composition different from that in the cisterna magna [12]. The existence of a consistent inhomogeneity of CSF acid-base content emphasizes the inaccuracy of using lumbar CSF pH to estimate ECF pH as a regulator of pulmonary ventilation and determinant of cerebral blood flow.

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M. C. Blayo, Maître de Recherches C.N.R.S.
Unité de Recherches de Réanimation
U 13 I.N.S.E.R.M. Hôpital Claude Bernard
10, Av. de la Porte d'Aubervilliers
F-75019 Paris
France