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Discussion

Plasma serotonin

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In view of the possible importance of plasma serotonin in clinical psychiatric and haematological research, two recent articles [1,2] require comment.

It has been known for many years that serotonin in whole blood is, to a large extent, sequestered in the platelets, as a consequence of an extremely active uptake process [3]. As long ago as 1954 [4] it was estimated that plasma serotonin concentration was 2 ng/ml and great care was taken to avoid rupture of platelets. Preparative procedures and sample containers have improved, and there appears to be less doubt about the reality of plasma serotonin concentrations, though the question of whether it is a measure of platelet fragility remains. If it is accepted that plasma serotonin exists as an entity apart from serotonin released from broken platelets, then it is, therefore, that portion which has not been taken up into the platelet or any other cell and may be free or protein-bound. Credible estimates of total plasma serotonin do show considerable variation from 0.39 ± 0.1 ng/ml [5] to 2.6 ± 0.9 ng/ml [6], but indicate that it constitutes a very small percentage of whole blood serotonin (140 ± 62 ng/ml [7], 126 ± 46 ng/ml [8] or 99 ± 11 ng/ml [9]).

Measurement of whole blood serotonin has frequently been taken to represent platelet serotonin [9,10] but should not be confused with it. Anderson *et al.* [7] made this point when they laid down theoretical definitions of plasma-, platelet-, cellular- and free-serotonin. Separate pools of serotonin were emphasised by Ortiz *et al.* [11] and again by Van Kempen [12] when he pointed out that an 'expression of plasma serotonin as ng/10^9 platelets' [13] was invalid. Despite these efforts, plasma serotonin continues to be misrepresented.

The plasma used as the source of serotonin in a recent paper [1] consisted of the supernatant obtained after centrifugation of blood at 700 *g* for 10 min, an almost ideal procedure for obtaining platelet rich plasma. After freezing at −70°C, thus breaking up the platelets and releasing serotonin, the plasma was subjected to ultrafiltration. The ultrafiltrate was then assayed for serotonin. The concentration was understandably quite high (43.86 ng/ml) and quite surely does not represent true plasma serotonin or plasma free serotonin. More importantly it is not clear exactly what the value does represent.

In the study by Keating *et al.* [2], the preparation of plasma is not detailed but the values of 121.2 ± 69.8 μg/l suggests that what was used was a platelet rich sample. For the purposes of their study the measure was satisfactory, but to name it plasma serotonin was inappropriate.

Whole blood or platelet-rich plasma serotonin concentrations are useful measures in terms of

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determining drug compliance or patient response to serotonin-uptake inhibitors. However, plasma free serotonin may represent the active serotonin in blood and could dictate the sensitivity of the receptors to which it has access. A reliable method for its assay is, therefore, essential but before that is possible, it is clear that there should be an accepted protocol for the preparation of the plasma source of serotonin, although it may yet be too early to dictate the conditions for the preparation of plasma free serotonin.

Our recommendation re-emphasises the suggestions of Anderson *et al.* [7] and is that when the concentration of serotonin in plasma is measured, two points must be taken into consideration in terms of the preparation of the plasma. These are that at no stage before obtaining cell-free plasma should the sample be frozen, and that the length and strength of the centrifugation of the whole blood or platelet-rich plasma should be such that it is rendered cell free.

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