Effect of low-dose dopamine on serum concentrations of prolactin in critically ill patients

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**Summary**

Dopamine is a naturally occurring catecholamine with actions in the central nervous system and endocrine systems, including inhibition of prolactin release from the pituitary gland. Prolactin secretion has been shown to be increased in response to physiological stress, while hypoprolactinaemia is associated with a reduction in the cellular immune response. We have investigated the effects of low-dose infusion of dopamine 2.5 μg kg⁻¹ min⁻¹ on serum concentrations of prolactin in critically ill patients. Six hours after commencing the dopamine infusion, mean serum prolactin concentration had decreased from 746.95 to 128.9 μg litre⁻¹ (normal range 84–488 μg litre⁻¹). This represented a mean reduction of 79.2%, with 35% of patients exhibiting a subnormal concentration while receiving dopamine. This reduction was reversed after cessation of dopamine and reproducible on re-institution. This suppression of the release of dopamine may be a detrimental side effect of low-dose dopamine infusion in critically ill patients. (Br. J. Anaesth. 1997; 78: 97–99)

**Key words**


Dopamine is a naturally occurring catecholamine, the immediate precursor of noradrenaline, which acts as a neurotransmitter in the central nervous system and is also secreted by the adrenal medulla. In addition, dopamine has effects on the hypothalamic-pituitary axis, being involved in the regulation of prolactin, growth hormone and thyroid stimulating hormone.

Dopamine acts on β₁ and to a lesser extent β₂ adrenergic receptors, α receptors and dopaminergic DA1 and DA2 receptors. Hence dopamine has inotropic, chronotropic and vasoconstrictor properties via adrenergic receptors, while by activation of DA1 receptors, dopamine can produce renal and splanchic vasodilatation. These effects are dose-dependent, with dopaminergic effects predominating at low dose (0.5–3.0 μg kg⁻¹ min⁻¹).¹

Low-dose dopamine is used commonly for its renal vasodilating property in critically ill patient, to maintain renal blood flow, glomerular filtration rate and urine output. However, there is no evidence that incipient renal failure can be aborted, or outcome modified, while arrhythmia, myocardial ischaemia, depression of respiratory drive, increased intrapulmonary shunting and digital necrosis have been reported as side effects of dopamine.² Therefore, the continued use of dopamine to “protect” the kidneys must be viewed critically.

The release of prolactin from the pituitary gland is regulated by both the reproductive hormones and central nervous system amines, including dopamine, acting via DA2 receptors on lactograph cells. Stress, surgery and a variety of anaesthetic drugs, including opioids, also increase serum concentrations of prolactin.³

Prolactin has been shown to be an immunoregulatory hormone, and hypoprolactinaemia may compromise cellular immune function. In mice, dopamine agonists suppress T-cell-dependent induction of macrophage tumour killing activity and lymphocyte proliferation, while co-administration of prolactin reverses these effects.⁴ Devins and colleagues,⁵ using dopamine infusions of > 5 μg kg⁻¹ min⁻¹, have shown greater than 90% reduction in serum prolactin concentration, with an immediate, but transitory decrease in T-cell response and lymphocyte count. These were reversible after cessation of dopamine. Similarly, data from critically ill infants and children showed that dopamine induced suppression of prolactin release, which is of particular concern as hypoprolactinaemia has been associated with poor clinical outcome in preterm infants through effects on surfactant synthesis, water regulation and gastrointestinal maturation.⁶

The aim of this study was to assess the effect of low “renal” dose dopamine on serum concentrations of prolactin.

**Methods and results**

After obtaining local Ethics Committee approval, all adult patients admitted to our intensive care unit...
surement because of hypotension (systolic arterial pressure < 2 h) or considered to be at risk of renal impair-
concentration, using an Immulite Prolactin
frozen and analysed in batches for serum prolactin
obtained 6 h later. All samples were separated,
menced and the final serum sample (sample 4) was
obtained. Dopamine infusion was then recom-
was obtained and dopamine infusion discontinued
after 6 h, serum sample 2 was obtained and dopamine
infusion was recommenced as required. After 6 h, serum sample 2 was obtained and dopamine infusion discontinued for another 6 h. After this time serum sample 3 was obtained. Dopamine infusion was then recom-
menced and the final serum sample (sample 4) was obtained 6 h later. All samples were separated, frozen and analysed in batches for serum prolactin concentration, using an Immulite Prolactin Chemiluminescent Enzyme Immunoassay System (Diagnostic Products Corp., LA, USA).

The results were analysed using a paired t test.
The study did not involve administration of dopamine to any patient who would not normally have received the drug in their management in our ICU. Any patient who developed oliguria or anuria which did not respond to i.v. fluids, correction of hypotension and i.v. diuretic was recommenced on dopamine infusion and removed from the study.

During the 3-month period, December 1995 to March 1996, 82 patients were admitted to the ICU, of whom 20 (seven female) were included in the study. Age ranged from 16 to 83 yr (mean 60.3 yr) and patients had a median APACHE II score of 18.5 (range 10–24). Two other patients died within 18 h of admission to the study and their results were excluded.

Mean serum prolactin concentration was 746.95 mu. litre\(^{-1}\) (95% confidence interval 532–962 mu. litre\(^{-1}\)) before commencement of dopamine, with 60% of patients having a supranormal level (normal range 84–488 mu. litre\(^{-1}\)). After 6 h of dopamine infusion, there was a reduction in serum prolactin concentration in all patients by a mean of 79.2 (SD 12.5) % (fig. 1). At this time, 35% of patients exhibited a subnormal serum prolactin concentra-
However, this reduction was reversed after cessation of the dopamine infusion for 6 h, with an increase to supranormal levels in 70% of patients. After another 6 h of low-dose dopamine, mean serum concentration of prolactin decreased again, by 83.9 (10.3) %, with 50% of patients exhibiting concentrations less than the normal range.

Measured changes in serum prolactin concentra-
tion were all statistically significant at the \(P<0.001\) level.

Comment

The results of this study demonstrate that low
(renal) dose dopamine (2.5 \(\mu g\) kg\(^{-1}\) min\(^{-1}\)) markedly reduced serum concentrations of pro-
lactin. This effect was both reversible after cessation of dopamine and reproducible after its recommence-
ment. These findings are in accordance with those of
other workers\(^5\,6\) who used twice the rate of infusion used in this study. Indeed, the magnitude of sup-
pression of serum prolactin in our study was almost as great as that found by Devins and colleagues\(^5\) (79–84% compared with greater than 90%), despite using a lower dose.

It is interesting to note that without dopamine, 60–70% of patients exhibited supranormal prolactin concentra-
tion levels, whereas with dopamine, serum prolactin concentration decreased to normal and even subnormal concentrations. Prolactin is an immunomodulatory hormone involved in the endocrine response to stress and consequently, any suppression of cellular immunity associated with a reduction in serum prolactin would be undesirable and may predispose critically ill patients to infective complications. Therefore, it seems that in the absence of controlled clinical trials confirming the efficacy of low-dose dopamine as a renal protective agent, its continued use for this purpose should be questioned.

Acknowledgements

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References

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