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Management of Hypertensive Emergencies in Children

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The emergency management of severe hypertension in a child includes careful clinical assessment before embarking on specific drug treatment. In particular, consideration of the degree of systemic illness, and the relative likelihood of specific causes of the hypertension, will usually warrant multi-discliplinary care, often within the intensive therapy unit. Intravenous labetalol and sodium nitroprusside are commonly used in this situation, but more recently intravenous nicardipine has also been found to be valuable. Oral short-acting nifedipine can be given, but its use is controversial as the effect is less predictable. Whichever drug is prescribed, the aim is to reduce blood pressure slowly with careful blood pressure monitoring, as the complications of a precipitate drop in blood pressure are as serious as those of severe hypertension.

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Introduction

Hypertensive emergencies are uncommon in paediatric practice. When faced with this problem, a working knowledge of the principles of management is more important than that of the specific features of the drugs used.

A background understanding of blood pressure (BP) variation in childhood will make management more appropriate. Genetic variability and environmental factors both have a role in determining an individual's BP, which is dependent on height more directly than age or other parameters of size. Measurement of BP is unfortunately relatively infrequently performed in children. Measuring equipment is often poorly maintained and the situation is now confounded by the withdrawal of mercury sphygmomanometers for safety and environmental concerns[1]. Technique is important. The child should be resting and the measuring cuff (bladder-size) should cover at least 2/3 of the upper arm length. Automated methods are often unreliable and machines must be well-calibrated. Always verify the reading yourself, if possible on more than one occasion. Invasive measurement is often very useful but not always appropriate. Beware of the "silent gap" if BP is very high. Mean BP can be used if available but, particularly in young children, the diastolic BP is often not easily measurable. Systolic BP is usually the most reliable parameter for monitoring purposes.

Hypertension

Charts of normal BP are available[2]. However "hypertension" in childhood is poorly defined: for example >95th centile, 10mmHg above 95th centile, and >99th centile are all used variably[3]. Table 1 shows values for "significant" and "severe" hypertension, which may be used in clinical practice as a rough guideline to BP levels which should be investigated and managed effectively[4].

A hypertensive emergency exists when there is organ damage, or impending organ damage, and is not defined in terms of the BP level, as this in itself cannot predict the severity of the problem alone[5,6]. The term hypertensive "urgency" is

Table 1. Rough guide of hypertension values in childhood				
Age	Significant hypertension		Severe hypertension	
	Systolic	Diastolic	Systolic	Diastolic
7 days	96		106	
<1 month	104		110	
<2 years	112	74	118	82
3–5 years	116	76	124	84
6–9 years	122	78	130	86
10–12 years	126	82	134	90
13–15 years	136	86	144	92
16–18 years	142	92	150	98

sometimes used[7,8] to distinguish those cases without organ damage, but with a possibility of such damage occurring in the next day or so. In practice this exact distinction is not often possible. The organs susceptible to damage include the brain, eyes, heart and kidney, with the major pathological process being fibrinoid necrosis of arterioles.

"Essential" hypertension is a poorly defined entity in children. Severe hypertension should always initially be considered to be "secondary" in cause. Causes of hypertensive emergencies include (in rough order of frequency) reflux nephropathy, obstructive uropathy, renovascular disease, glomerular disease, polycystic kidney disease, haemolytic-uraemic syndrome, coarctation, phaeochromocytoma, Wilm's tumour, renal dysplasia, intracranial disease and drugs[9]. Thus, renal causes predominate.

Often there are no symptoms even in severe hypertension[9]. If present, these are mainly neurological: visual symptoms, facial palsy, convulsions, hemiplegia and frank hypertensive encephalopathy. Cardiac failure is more commonly found in very young children in whom neurological complications are relatively rare.

Management

It is worth restating that the principles of the management of hypertensive emergencies are at least as important as the specifics of the drugs used. Appropriate intensive care facilities should be available. In the emergency evaluation one should assess cardiovascular status both clinically and with an ECG. Echocardiography is particularly helpful in assessing left ventricular function. Neurological status (conscious level, irritability, fits) will often determine the level of medical and nursing care required. Assessment of fluid balance and renal function will also influence treatment profoundly. An ophthalmological opinion is valuable. Thus, a multi-disciplinary approach is appropriate.

Beware of hypovolaemia. This can cause or exacerbate hypertension[10]. Also, it is sometimes difficult to decide whether fits in the presence of hypertension are the cause or an effect. In a post-ictal patient, the magnitude of BP increase has been found to be a useful clinical parameter to exclude a hypertensive crisis[11].

Treatment must be based on the cause if known or suspected. In renal disease intravascular fluid ("saline") overload is often under-estimated, and tissue oedema is not well correlated with intravascular volume. Thus the drug of choice may be a diuretic in the infant or child whose main problem is systemic fluid overload, with hypertension as part of the clinical picture. Renal function will profoundly influence management, particularly use of drugs. Urine output should be monitored and, if serum creatinine is outside the normal range, caution given in the use of drugs excreted though the renal route. Renal dialysis or filtration may be required. Renin-dependent causes will influence the use of ACE-inhibitors, particularly if renovascular. Catecholamine-driven hypertension needs specialist advice regarding both α-adrenergic and β-blockade, with particular attention to problems around surgery for phaeochromocytoma.

Consideration of the length of time over which the hypertension has developed is very important[12]. Cerebral autoregulation keeps cerebral blood flow relatively constant within systemic BP limits but over time this range is altered in hypertension. If BP is lowered too rapidly there is a real danger of relative hypotensive damage to watershed areas, particularly visual cortex, cerebellum and end-arteries (ciliary arteries to optic nerve and spinal

Table 2. Drug doses for hypertensive emergencies (start with the lower doses)		
Drug	**Route**	**Dose**
Sodium nitroprusside	IV	0.5–8 microg/kg/min
Labetalol	IV	0.25–1.5 mg/kg/hr
Nifedipine	Oral	0.1–0.25 mg/kg/dose (initial doses)
Nicardipine	IV	1–3 microg/kg/min
Diazoxide	IV	1–3 mg/kg/dose

arteries). Visual loss may be permanent. Thus, the principle of slow reduction of severe, chronic hypertension is paramount.

Drug therapy

The specific drugs most widely recommended for initial emergency management are sodium nitroprusside and labetalol. Other drugs that have also been recommended include nifedipine, nicardipine and diazoxide. These are discussed individually below, and doses are given in Table 2. However, whichever drug is used, the principle of the slow reduction in blood pressure is the same. A helpful goal to strive for is to aim to reduce BP initially by only a third of the difference between the acute BP level and the appropriate normal value. Only after the first 24 hours or more should it be attempted to reduce BP further with the gradual addition of longer-acting drugs. Whichever agent is used, frequent and reliable BP monitoring is necessary. An intravenous saline infusion should be available to raise BP if it has dropped too low.

Sodium nitroprusside

Sodium nitroprusside is a potent vasodilator with an almost instant effect when given intravenously. It is also very short-acting (seconds) and therefore capable of exquisite BP control. Continuous BP monitoring is mandatory. The drug undergoes rapid photo-degradation so the solution must be covered with aluminium foil. *In vivo*, cyanide is produced from its local breakdown in smooth muscle, which is then metabolised to thiocyanate in the liver. This is excreted by the kidney. Therefore it must be used with caution in patients with renal or hepatic failure. In the absence of organ failure, a clinical problem should not be expected unless the drug is used for more than 48 hours or so. After this time a worsening metabolic acidosis can be anticipated. It may be possible to measure thiocyanate levels in these circumstances, but usually the patient will be suitable for longer-acting drugs by this time.

Labetalol

Labetalol is also commonly used in the acute situation. Most of its action is via β-adrenergic blockade but there is also α-adrenergic blockade (15%). It therefore reduces cardiac output and causes peripheral vasodilatation. It has a rapid onset but a longer duration of action (hours) and is therefore not capable of such sensitive BP regulation as nitroprusside. Its use is limited if there is clinical evidence of cardiac failure as it may further lower cardiac output. Like other β-blockers, there must be caution in asthmatics. It is metabolised in the liver and its use is not limited in renal failure. Initial incremental loading doses of 250 microg/kg (up to 1 mg/kg) have been recommended followed by an infusion of 0.25–1.5 mg/kg/h[13].

Nifedipine

The use of nifedipine in the acute phase is controversial[14]. In adults, its use has been associated with extreme hypotension and neurological effects. However, in children this has rarely been reported and a recent series endorses its safety in children when used appropriately[15]. Its action is by vasodilatation. Cardiac output is maintained but there is often a reflex tachycardia, which in adults certainly may lead to myocardial or cerebral ischaemia. Headaches and flushing are common. Many paediatric centres use this drug in an otherwise well child and in small, frequent doses (initially 100–250 microg/kg). Subsequently larger doses may be appropriate, when the child has demonstrated that initial doses have not caused a precipitate drop in BP. Small doses can be extracted from the capsules and the effect can be quite rapid, starting within 10 minutes. Unfortunately with the difficulty in accurately measuring the small doses of liquid from the capsules, dosing errors may occur and care needs to be taken[16]. The duration of effect and potency when used in this way is unpredictable, particularly when absorption is variably sublingual and from the stomach and small bowel, but the longer-acting (sustained-release) preparations are not suitable in the immediate emergency situation. Unfortunately nifedipine in this context illustrates the difficulty in administering medicines in small doses to children when the formulations available are really suitable only for larger individuals.

Nicardipine

Recently an intravenously administered calcium-channel antagonist, nicardipine, has become available. Although there is limited experience with its use in paediatric practice, reports of its suitability have been favourable[17], and it is increasingly being used for children. It has a very rapid onset of action, within a few minutes, and a relatively short duration of action (half-life 40 minutes). Advantages over nitroprusside include the ability to use it for more than a few days, as it does not produce toxic metabolites. In a recent study[18], when used in doses gradually increasing to 3 microg/kg/min, nicardipine only occasionally caused unwarranted hypotension and this was readily improved by stopping the drug. Intravenous calcium can also be used in situations of hypotension and reduced cardiac output (0.2 ml/kg i.v. in the form of 10% calcium chloride over 5 minutes)[19].

Diazoxide

For many years, diazoxide was the most frequently used drug for hypertensive emergencies. Its use has decreased as other drugs have become available. It has unpredictable potency and is associated with the complications relating to over-rapid reduction of blood pressure. However, it still can be useful if used in small, frequent doses (1–3 mg/kg/dose) rather than the large boluses employed in the past. There is a risk of hyperglycaemia and a maximum total dose of no more than 10 mg/kg per 24 hours is generally recommended.

Other drugs

Intravenous hydralazine is no longer indicated in the emergency situation now that drugs with more predictable potency and fewer side effects are available. Mention should be made of the ACE-inhibitors so as to emphasise that they are not usually suitable for use in an emergency – the magnitude of their effect is dependent on renin-status and they are particularly potent in renovascular disease. Their effects are therefore unpredictable, particularly if the cause of the hypertension is unknown. In unilateral renal vascular disease there is the very real risk of infarction of the affected kidney.

In the second phase of management there is gradual reduction of short-acting drugs and gradual introduction of oral longer-acting drugs. At this stage, it is still important not to reduce BP too quickly. Usually more than one drug is used, for example a β-blocker, diuretic and vasodilator. Success depends on a good knowledge of the treatment of hypertension generally and will usually require an appropriate specialist.

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