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Case series: propranolol liquid in the treatment of tachyarrhythmias in neonates and infants: potential for errors

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Brief Report

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Abstract

Oral propranolol therapy is commonly used for the prevention of tachyarrhythmias in infancy and childhood. Propranolol is commercially produced in four concentrations allowing varying volumes to be administered. However, quite often an alternative strength of propranolol liquid is issued without clear change in instructions or warning. This may lead to parents inadvertently administering the wrong dose.

Oral beta-blocker therapy is often the first-line antiarrhythmic pharmacological therapy used to prevent neonatal and infantile tachyarrhythmias.[1] Propranolol may be used either solely or in combination with other antiarrhythmic agents for the management of supraventricular tachycardia and ventricular tachycardia. Propranolol liquid is commercially produced in varying strengths in the United Kingdom.[2] Dosing is calculated based on weight, incrementally increased with growth, then titrated against clinical effect, electrocardiogram, and complications.

Quite often alternative strengths of propranolol liquid are issued without clear change in instructions or warning of the correct volume to administer. This may lead to parents inadvertently administering the wrong dose, by almost a factor of 10, a common mistake when administering children's medications.[3] We describe a small series of such infants.

Case 1

A baby born via emergency caesarean section at 38 weeks gestation due to foetal tachycardia was subsequently diagnosed with persistent junctional reciprocating tachycardia. He was discharged with dual pharmacological therapy including amiodarone (100 mg/5 ml) and propranolol liquid 3.5 mg three times a day. Instructions for parents were provided to administer 0.35 ml three times a day (50 mg/5 ml) propranolol liquid. When he was seen in the outpatient clinic 5 months later, it was noted that the local propranolol preparation prescribed was 10 mg/5 ml concentration with instructions given to administer 1.75 ml; however, his mother had not realised there was a difference in concentration and had continued to administer propranolol 0.35 ml. This resulted in him receiving 0.7 mg rather than the intended 3.5 mg. The prescription of amiodarone prescribed locally was also half the strength of that initially prescribed, resulting in 50% of the intended dose being administered. The baby was well but Holter monitoring revealed persistent junctional reciprocating tachycardia, likely because of inadequate antiarrhythmic pharmacological control. Following discussion with the general practitioner, local prescribing of propranolol was continued using a 10 mg/5 ml solution, with clear instruction provided to administer 1.75 ml. Amiodarone 100 mg/5 ml was also prescribed with the correct volume of amiodarone administered. Subsequent Holter monitoring demonstrated sinus rhythm with control of persistent junctional reciprocating tachycardia.

Case 2

A baby was born by emergency caesarean section for foetal tachycardia at 36-week gestation, requiring cardiopulmonary resuscitation at birth, followed by admission to paediatric intensive care due to a diagnosis of persistent junctional reciprocating tachycardia, resulting in impaired biventricular systolic function. He was discharged home with dual pharmacological therapy including amiodarone liquid 20 mg once daily (1 ml) and propranolol liquid 3 mg three times a day (0.3 ml). At a subsequent outpatient appointment, following incremental dose increases in line with weight gain (5 mg, 7.5 mg, and 12 mg), clarification of the volume of propranolol being administered was sought by the consultant as it was documented that he was taking 12 mg three times a day with the plan to increase this to 15 mg. His mother reported giving 0.24 ml of a 50 mg/5 ml solution equating to 2.4 mg instead of 15 mg, thus receiving a suboptimal dose of

Table 1. Cost comparison of propranolol longevity per bottle

Comparison of propranolol longevity per 150ml bottle for a 6-kg child (based on 500 mcg/kg TDS dose)				
Dose to be given	50 mg / 5 ml	40 mg / 5 ml	10 mg / 5 ml	5 mg / 5 ml
3 mg TDS	166 days	133 days	33 days	16 days

ml = millilitres; kg = kilograms; mcg = microgram; TDS = three times a day.

Table 2. Dose ranges and volumes per weight and propranolol solution

Comparison of propranolol doses and volumes administered with different propranolol solutions					
		Dose to be administered			
Weight of child	Propranolol dose calculated at 500 mcg/kg	Propranolol 50 mg / 5 ml	Propranolol 40 mg / 5 ml	Propranolol 10 mg / 5 ml	Propranolol 5 mg / 5 ml
3 kg	1.5 mg	0.15 ml	0.1875 ml	0.75 ml	1.5 ml
6 kg	3 mg	0.3 ml	0.375 ml	1.5 ml	3 ml
9 kg	4.5 mg	0.45 ml	0.5625 ml	2.25 ml	4.5 ml

mcg = micrograms; kg = kilograms; mg = milligrams; ml = millilitres.

propranolol. It was unclear when the change in volume had been initiated; however, the result was uncontrolled persistent junctional reciprocating tachycardia administered. A new prescription and bottle of propranolol was provided with the instruction clearly labelled to give 1.5 ml. Parents were given advice about checking future prescriptions with the general practitioner and local pharmacist and to contact the cardiac team if prescriptions changed without notification from the cardiac team. Written confirmation was sent to the general practitioner highlighting the dosing error. Repeat Holter monitoring demonstrated the control of persistent junctional reciprocating tachycardia.

Case 3

An infant with a diagnosis of atrioventricular re-entry tachycardia was prescribed propranolol 5 ml three times a day, rather than being prescribed in milligrams. The infant was given 5 ml of propranolol liquid (5 mg/5 ml) at home (5 mg) but was provided with propranolol liquid 50 mg/5 ml, labelled as 5 ml, as per instructions from the general practitioner. The mother called the paediatric outpatient department reporting the infant to be very sleepy. An outpatient appointment was arranged for the following day. Electrocardiogram changes showed the infant to be bradycardic. On further questioning, it was revealed that a stronger concentration had been provided and the infant had received a 10-fold overdose (50 mg). The infant was admitted for overnight monitoring with propranolol re-initiated once the heart rate normalised. A new bottle of propranolol was provided with the dose, volume to administer, and the strength of the solution clearly labelled on the bottle, with notification sent to the general practitioner highlighting the error. Parents were also educated before discharge home about checking the labels of locally acquired bottles of propranolol to ensure doses remained accurate.

Discussion

Administration of medication to babies can be a challenge. Parents need to ensure accurate amounts of liquid have been swallowed.[4,5] This can be particularly taxing with larger volumes, especially if medication is spat out or vomited. To assist, delivery manufacturers have made propranolol liquid available in a range of concentrations allowing smaller volumes to be administered. Smaller volumes delivered to the back of the mouth by syringe are less likely to be expelled.

Current practice in the tertiary cardiac centre is to prescribe propranolol manufactured at a concentration of 50 mg/5 ml. Babies commenced on propranolol therapy are given a letter detailing the strength of propranolol provided on discharge, that is, (50 mg/5 ml), with details of the manufacturer so that local prescriptions can be easily sourced and dosing errors avoided. Additionally, the liquid is labelled with both the strength in milligrams and measurement in millimetres to avoid confusion.

Propranolol liquid is available in 4 different strengths, produced by 10 different suppliers with similar pricing structure. The net cost per 150 ml bottle is 50 mg / 5 ml = £43.83, 40 mg / 5 ml = £44.72, 10 mg / 5 ml = £33.06, and 5 mg / 5 ml = £26.77.[6] The dose range of propranolol for neonates in the United Kingdom is usually 250–500 µg/kg three times a day; however, dosing to a maximum of 1 mg/kg, adjusted according to response is often required[3].

Propranolol 5 mg/5 ml solution appears to be commonly prescribed in the community and by some paediatricians in secondary care, likely because it appears cheaper. Personal communication with professionals in primary care has highlighted that their electronic prescribing systems usually opt for cheaper and more dilute preparations as first line.

For a child requiring a dose of 3 mg three times a day, it is more cost-effective to prescribe a bottle of 50 mg/5 ml (£43.83), lasting 166 days – Table 1. Prescribing 5 mg /5 ml bottles provides a false economy as 10 bottles are needed for the same time frame at a cost of **£267.70**. In addition, the volume to administer is 10 times that of the more concentrated solution; 3 ml versus 0.3 ml comparison is shown in Table 2. There is also a shelf life of 3 months to consider when prescribing propranolol liquid. Depending on the dose and volume to be administered, the bottle may expire before completion requiring a new prescription; however, this would still represent a cost saving, if prescribing the 50 mg/5 ml solution.

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Conclusions

Drug errors in children, particularly those under the age of 4 years, is a recognised problem accounting for 10% of reported medication incidents, 5.6% of these resulting in hospital admission.[7,8] The variation in propranolol liquid preparations, the differing prescribing practices in secondary and primary care, and the large number of suppliers considerably complicates accurate administration and has led to some serious drug errors. Although none of our infants suffered any long-term harm, confusion over changes in concentration resulted in the wrong dose being administered, which might result in dangerous consequences. Where possible, standard concentrations should be agreed between primary, secondary, and tertiary care providers to reduce the potential for error.[9] The exact dose in milligrams, millilitres, and the concentration of the preparation should be checked carefully with parents/carer at each appointment. Confirmation of the dose and strength of propranolol liquid, including any dose changes, should be highlighted and included in documentation to local professionals including general practitioners and paediatricians. Parents should also be provided with advice about who to contact at the cardiac centre, if unexpected changes are made to prescriptions provided locally.

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Conflicts of interest. None.

Ethical standards. Not applicable.

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