CASE REPORT

# Renal failure caused by eyedrops containing phenylephrine in a case of retinopathy of prematurity

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**Abstract : The patient was a low birth weight infant with a history of renal failure. She was referred to our department 29 days after birth to undergo fundus examination. She experienced renal failure after undergoing a mydriatic test and needed medical treatment. Eyedrops containing phenylephrine were instilled several times and additional drops were also instilled during the fundal examination using an eyelid retractor, therefore the blood concentration of the drug was elevated sufficiently to contract the renal vessels, ultimately inducing renal failure. The present case suggests that since the use of mydriatic eyedrops in low birth weight infants could induce renal failure, the following points should be considered : 1) Mydriatic eyedrops should be used with caution by monitoring mydriasis and avoiding excessive instillation ; 2) After instillation, the lacrimal region should be compressed to prevent the flow of mydriatic drops to the nasolacrimal canal ; and 3) Vital signs should be monitored to check the onset of any adverse reactions for 12 hours after fundal examination. J. Med. Invest. 50 : 203-206, 2003**

***Keywords*** **:** *Renal failure, mydriatic drug, phenylephrine, retinopathy of prematurity*

## INTRODUCTION

Due to recent advances in neonatal care, the chance of survival for low birth weight infants has improved. However, the prevalence of premature retinopathy has increased. The first area of the retina affected by premature retinopathy is the peripheral region, and fundal examination using a mydriatic drug is therefore essential.

Systemic adverse reactions associated with the instillation of mydriatic eyedrops include hypertension and bradycardia (1, 2). However renal failure has not been reported previously. This paper presents a case of premature retinopathy who showed renal failure after mydriatic tests.

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## CASE REPORT

Patient : A 29-day-old female weighing 674g. History of present illness : In May, 1999, super low birth weight twins(690g) were delivered after 26 weeks and 3 days of gestation. The patient was referred to our department 29 days after birth to undergo fundal examination. Past medical history : On days 4 and 5 after birth, indomethacin sodium was administered intravenously to treat patent ductus arteriosus, and then the patient suffered acute renal failure. Family medical history : The other twin, an older brother, was also a super low birth weight infant, weighing 964g. Findings on initial examination : Fundal examination was performed using

a mydriatic eyedrop (Mydrin-P®). A broad circumferential avascular zone was observed in both eyes, and the patient was therefore diagnosed as premature retinopathy. Course (Figure 1) : On day 36, the patient was diagnosed as stage 1, following the international classification for premature retinopathy. On day 43, clinical staging therefore advanced to stage 2. The ocular fundi were difficult to examine clearly due to poor mydriasis and hazy media.

On day 46, a thorough fundal examination was performed by instilling more drops of a mydriatic drug (Mydrin-P®). On the next day, urine volume decreased. On day 48, the patient's general condition worsened and the number of apneic episodes increased. Consequently, the patient was placed on respiratory management by nasal continuous positive airway pressure (NCPAP). Decreased urine volume was treated by restricting water intake and administering a diuretic drug and dopamine.

On day 50, further fundus examination was performed. Mydrin-P® was again used and additional drops were instilled during the examination. On day 51, anuresis was confirmed and continuous dopamine infusion was initiated following the diagnosis of acute renal failure. A diuretic was administered intravenously on several occasions. In addition, the patient was intubated for artificial respiration management to avoid apnea. Since the patient experienced renal failure after the instillation of Mydrin-P®, excessive usage of the mydriatic drops was suggested to be the cause. As a result, in subsequent fundus examinations, the use of Mydrin-P® was restricted and the pupil was allowed to dilate with time. The patient did not experience further renal failure thereafter.

Several laser coagulation therapies improved clinical staging of premature retinopathy to stage 3.

## DISCUSSION

Mydriatic eyedrops are normally used for routine fundus examination. Mydriasis is essential for premature retinopathy patients, since the periphery of the ocular fundus needs to be examined. Mydriatic eyedrops are roughly divided into two types : parasympathetic blockers and sympathetic stimulants. The former directly or indirectly affects the pupillary sphincter muscle, whereas the latter directly or indirectly affects the pupillary dilator muscle.

Commonly used drugs for mydriasis include: tropicamide, atropine, cyclopentolate (parasympathetic blockers) and phenylephrine (sympathetic stimulant).

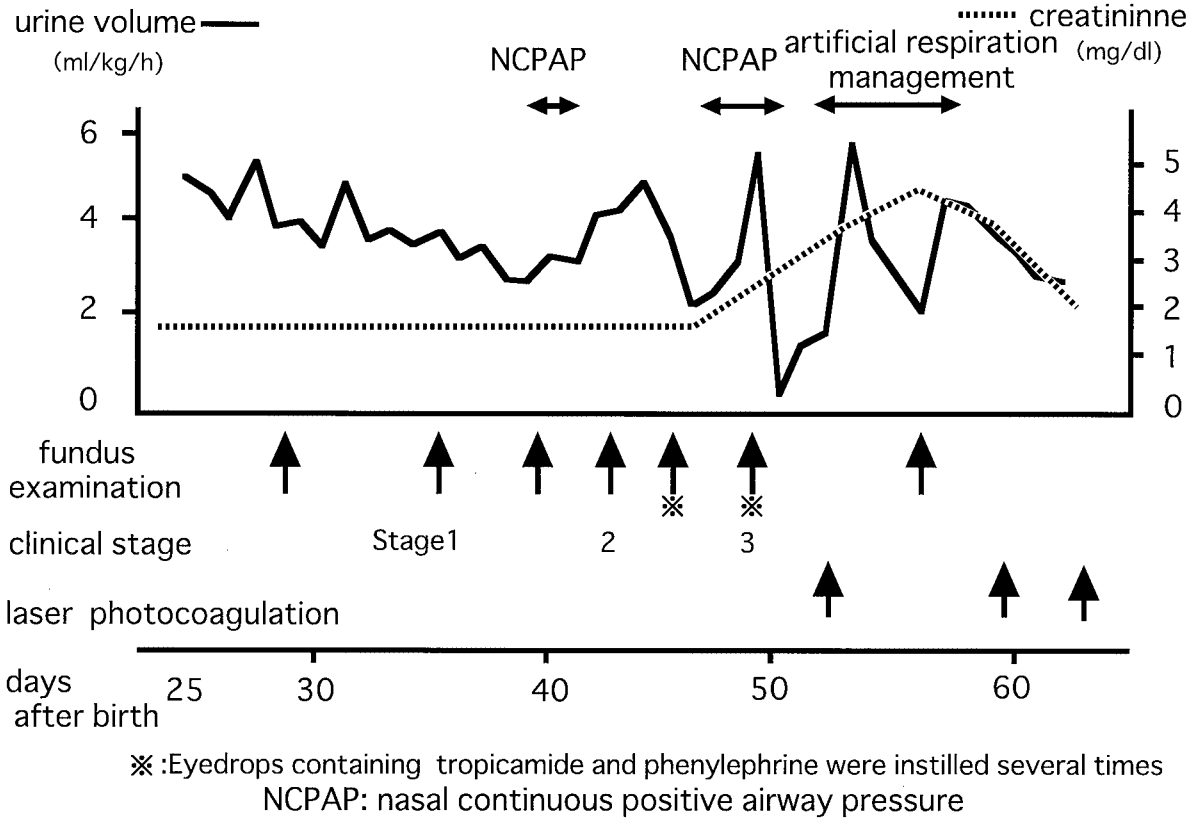


**Figure 1 : Laboratory data, clinical stages and the management**

Mydrin-P® is an eyedrop containing 0.5% tropicamide and 0.5% phenylephrine hydrochloride. Since this is a fast-acting and long-lasting drug, it is often utilized in mydriasis tests.

Tropicamide is a muscarinic antagonist that exerts little effect on the circulatory system. Although mydriatic drugs have been shown to cause adverse reactions in neonates and low birth weight infants such as bradycardia, few cases requiring special procedures have been reported (3). Phenylephrine is a potent α1-adrenergic receptor stimulant that acts on the cardiovascular system to increase blood pressure, lower heart rate, and constrict blood vessels in such organs as the kidney and the extremities to reduce blood flow (4, 5). Phenylephrine must therefore be administered with caution to patients with heart diseases such as hypertension, coronary disease or heart failure (6, 7).

Due to reports of bradycardia and apneic episodes, caution should be exercised when using Mydrin-P® in low birth weight infants by close monitoring and dilution of the drug as necessary (8).

Caputo *et al*. instilled10% phenylephrine in six neonates, for a total of three times with five minute intervals. They reported increases in systolic pressure by 10mmHg to 26mmHg and diastolic pressure by 2mmHg to 14 mmHg, while the heart rate decreased up to 20% in four neonates (1).

Rosales *et al*. instilled 2.5% phenylephrine and 0.5% tropicamide in ten low birth weight infants, weighing less than 1600g, for a total of three times with five minute intervals. An increase of greater than 20% in systolic pressure was observed in eight patients and an increase of greater than 50% was observed in three of these eight patients (2). Compared with adults, the effects of these drugs were reported to be greater in neonates, especially low birth weight infants, and due to immature cardiovascular and cerebrovascular systems, increased blood pressure is more likely to induce adverse reactions.

The development of the pupillary dilator muscle is incomplete in neonates, and several instillations are therefore necessary in dilating the pupil sufficiently (3). The tendency is that the more severe the prematurity, the more difficult mydriasis (9). In the present patient, the mydriatic drug was instilled many times due to poor mydriasis. This caused the accumulation of phenylephrine in the blood, constricting the renal vessels and thus resulting in renal failure.

When a mydriatic eyedrop is instilled, it enters not only the anterior chamber through the cornea, but also the blood through the conjunctiva, and the nasal mucosa and gastrointestinal tract through the nasolacrimal canal (10). On some mydriatic drugs, about 80% of administered dose is absorbed by the body (11). For example, under normal condition, 80% of timolol instilled to rabbits is absorbed by the body. Therefore, in order to increase the concentration of a mydriatic drug in the eye by blocking the flow of the drug to the nasolacrimal canal, compression of the lacrimal region and closure of the eyelids are recommended. Whitson *et al*. instilled 10% phenylephrine and reported that blood concentration 20 minutes after the instillation could be reduced by 15-19% by closing the eyelids for one minute (12). Most neonates will close their eyes after instillation of a mydriatic drug, but in the present patient, an eyelid retractor was used to instill eyedrop containing phenylephrine. As the result, the flow of this drug to the nasolacrimal canal was elevated, and blood concentration of phenylephrine therefore became high enough to cause renal failure.

Initially, we considered one possible explanation for the renal failure as follows: The fundus examination is very stressful for infants, and they sometimes experience apneic episodes after undergoing ophthalmological examination. To ensure sufficient cerebral blood flow after an apneic episode, the diving reflex constricts peripheral blood vessels, and this could lead to renal failure. However, assisted ventilation reduced the number of apneic episodes in the present patient when renal failure was exacerbated, thus negating the potential role of this possibility as the onset of renal failure.

The present patient was a low birth weight infant with a history of renal failure. When eyedrops containing 0.5% phenylephrine were instilled several times to dilate the pupil and the additional drops were instilled during the examination using an eyelid retractor, the blood concentration of the drug was elevated sufficiently to contract the renal vessels, ultimately inducing renal failure.

To the best of our knowledge, renal failure following the instillation of mydriatic eyedrops has not previously been reported. The present case suggests that since the use of mydriatic eyedrops in low birth weight infants could induce renal failure, the following points should be borne in mind:1) Mydriatic eyedrops should be used with the caution by monitoring mydriasis and avoiding excessive instillation ; 2) After instillation, the lacrimal region should be compressed to avoid the flow of mydriatic drops to the nasolacrimal canal ; and 3) Vital signs should be monitored to check the onset of any adverse reactions for 12 hours after fundal examination.

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