Urol Res (1982) 10:271–276

Urological Research

The Upper Urinary Tract Following a Ureteroneocystostomy (UNC) in Animal Experiments: I. Functional Findings

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Accepted: June 4, 1982

Summary. A ureteroneocystostomy (UNC) was carried out on 32 dogs. A standardised measurement of flow across the ureterovesical anastomosis revealed a significant obstruction on the day of the operation itself and on the first 5 days after the operation. On the 1st, 7th and 28th day after the operation there was no significant reduction in either tubulo-secretory or glomerular function on the operated and non-operated kidneys.

Key words: Antireflux-surgery, Postoperative obstruction to flow, Postoperative kidney function, Tubulo-secretory and glomerular partial function, Correlation between PAH and isotope clearance.

Introduction

Vesico-ureteric reflux (VUR) is a very common urological condition in children; surgical treatment by means of anti-refluxsurgery (ARS) is also correspondingly common, and is principally carried out by one of two methods: extravesical, without interrupting ureteric continuity [6, 10] or a combination of trans- and extra-vesical in the form of a ureteroneocystostomy (UNC) with diverse modifications [12; combination of all methods in 8].

The object of this study was to examine, by means of animal experiments, the function of the upper urinary tract following a unilateral ARS, both on the operated side and on the side which did not undergo surgery. The UNC was chosen as it is more commonly used than the extravesical ARS, on which subject material concerning animal experiments already exists [15].

Material and Methods

The experimental animals chosen were 32 female German shepherd dogs, mean bodyweight 27.5 kg (20–35 kg) and mean body length 112 cm (100–120 cm).

Anaesthesia was induced with Pentobarbital-Natrium[1] intravenously and after intubation ventilation was performed using a mixture of N_2O and oxygen in the ratio 1:3, volume of respiration 6 l min[2] while maintaining continual monitoring of pulse and blood pressure[3,4] as well as continuous analysis of the end-expiratory level of CO_2[5].

A radioisotope nephrogram and 131-J-Hippurate-clearance (OIH-Cl) (A–D series) were carried out preoperatively and on day 1 (B series), day 7 (C series) and day 28 (D series) postoperatively. The postoperative taking of urine from different sides for all clearances was carried out as in Fig. 2. The calculation of OIH–Cl was undertaken according to Britton and Brown (1971). The clearance which was not standardised had to be converted to kg bodyweight because a normogram for the surface area calculation in dogs only exists up to 22 kg bodyweight [4].

Operations

All dogs were operated on the right side according to the method of Politano and Leadbetter (1958). In order to measure the flow (series A) a nephropyelostomy as in Fig. 1 was carried out in addition.

Postoperative Tests of Function

Measurement of flow: The measurement of flow was performed directly after the operation and on postoperative days 1–7 as in Fig. 1 under standardised conditions (perfusate: 0.9% NaCl, height of the perfusate: 60 cm).

1 Nembutal®; manufactured by Deutsche Abbott, Ingelheim
2 Engström Respirator ER 321, System 300; manufactured by LKB medical AB Bromma, Sweden
3 Pressure Recorder Statham P 23 Db; manufactured by Statham, Hato Rey, Puerto Rico, USA
4 Meßbrücke Hellige MA 88K; manufactured by Hellige, Freiburg
5 CO_2-Spirometer URAS; manufactured by Hartmann & Braun, Frankfurt

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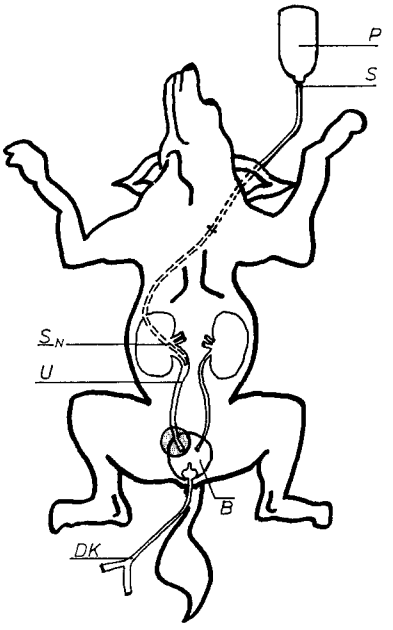

Fig. 1. Experimental arrangement for the flow measurement (series A). P = perfusate (500 ml 0.9% NaCl), S = level of the perfusate in all measurements 60 cm above kidney hight, S_n = pyelostomy, U = right ureter, B = bladder, DK = permanent bladder catheter. From: Heising (1980)

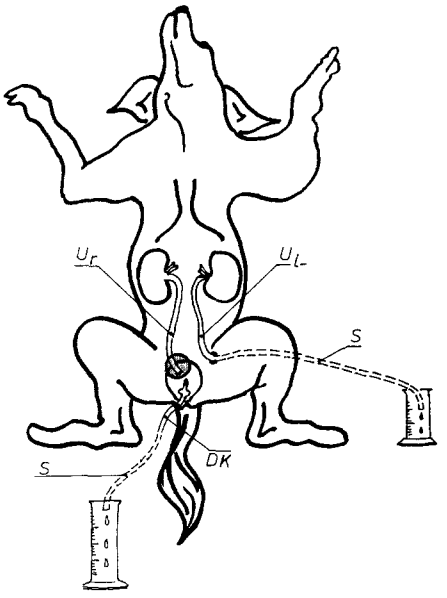

Fig. 2. Experimental arrangement for the side separated clearance (series B, C, D). U_r = right ureter, U_l = left ureter, S = catheter, DK = permanent bladder catheter. From: Heising (1980)

Table 1. Series A; flow rates following pyelostomy (PSt) or following PSt plus ARS, figures given in no. of drops/min (gtt/min)[c]. Modified according to Heising (1980)

Dog serial Nr.	Following PSt	Following ARS	Postoperative day 1–7 (d1–d7)							d1 PSt	d2 PSt	d3 PSt	d4 PSt	d5 PSt	d6 PSt	d7 PSt
			d1	d2	d3	d4	d5	d6	d7							
2	160	119	80	110	132	130	164	164	168	0.50	0.69	0.83	0.81	1.03	1.03	1.05
7	198	152	56	80	84	96	162	184	190	0.28	0.40	0.42	0.48	0.82	0.93	0.96
8	210	142	86	84	110	196	196	197	200	0.41	0.40	0.52	0.93	0.93	0.94	0.95
9	214	156	84	96	145	135	140	156	152	0.39	0.45	0.68	0.63	0.65	0.73	0.71
10	168	124	70	83	90	96	146	156	156	0.42	0.49	0.54	0.57	0.87	0.93	0.93
11	196	136	101	96	148	184	188	184	182	0.52	0.49	0.76	0.94	0.96	0.94	0.93
19	158	122	86	91	101	102	112	112	126	0.54	0.58	0.64	0.55	0.71	0.71	0.80
21	176	120	92	104	100	104	168	163	168	0.52	0.59	0.57	0.59	0.95	0.93	0.95
$\bar{x}$	185	133[a]	82[a]	93[a]	114[a]	130[a]	159[a]	164	168	0.45	0.50	0.62	0.70	0.87	0.89	0.91
±[b]	22	16	14	11	25	40	27	26	23							

[a] Significantly different (reduced) in contrast to (PSt)
[b] Rounded off to full figures
[c] Flow rate through a pyelostomy catheter ex situ: 300 gtt/min

Clearances

In addition to the OIH–Cl (see above) a simultaneous PAH and Inulin Clearance were carried out[6] at three different postoperative intervals: short term (day 1, 7) and middle term (day 28).

6 OIH–Cl using o-iodhippuric acid (^{131}J)-Na-Salt; manufactured by Amersham, Buchler, Braunschweig using the Radioisotope Camera Sigma 401, manufactured by Ohio-Nuclear Inc., Solon Ohio, USA, as well as a tandem arranged Philips processing and display system, types 9,812,307; 9,812,300; 98,123,301; manufactured by Philips, Eindhoven. The PAH and Inulin clearance were practised according to Balint (1965)

Statistics

The analysis of variants was conducted according to Scheffé (1954) using the following models:

Model I: $Y_{ijk} = \mu + \alpha_i + B_{ij} + \gamma_k + (\alpha\gamma)_{ik} + \epsilon_{ijk}$

Calculated according to this model were:

1. The differences of the OIH overall clearance, pre- and postoperatively, with the signification as follows:

μ = general average value
α_i = effect of the group i
B_{ij} = effect of the animal j of the group i
γ_k = effect before versus after surgery
$(\alpha\gamma)$ = associated reciprocity
ϵ_{ijk} = experimental error, normally distributed and independently presumed

2. The side-separated distribution of the total postoperative output of OIH, PAH and Inulin with the significantion

γ_k = clearance substance K, other factors as above.

3. The differences in the measured values of OIH, PAH and Inulin at the three postoperative intervals with the signification

γ_k = influence of the right or left side.

Model II served to calculate the significance of the differing flow rates:

$Y_{ij} = \mu + \alpha_i + B_j + \epsilon_{ij}$, signifies here:

μ = general average value
α_i = time when measured
B_j = animal within the group
ϵ_{ij} = experimental error as in model I.

The differing measured values of the individual clearance substances at the various points in time were calculated according to model III:

$$Y_{ijkl} = \mu + \alpha_i + B_{ij} + C_{ijk} + \delta_1 + (\alpha\delta)_{il} + (\alpha B\delta)_{ijl} + \epsilon_{ijkl}$$

In this signified:
μ = general average value
α_i = effect of the group
B_{ij} = effect of the animal within the group
C_{ijk} = effect of the k point in time for the j animal in the i group
δ_1 = effect of the side
ϵ_{ijkl} = experimental error normally distributed and independently presumed
$(\alpha\delta)$ respectively $(\alpha B\delta)$ correspond to the respective reciprocity.

Results

Blockage of excretion: Nephropyelostomy (PSt) *plus* ARS caused a significant decrease of flow from the ipsilateral kidney (Table 1) on the same side both immediately postoperatively as well as on days 1–5 postoperatively. The decrease of flow was not significant either after the PSt alone or on days 6–7, postoperatively.

Clearances: The simultaneous OIH, PAH and Inulin clearances were analysed on the postoperative days 1 (B series, Table 2), 7 (C series, Table 3) and 28 (D series, Table 4). Table 5 provides a comparison of the results. Extending the results represented in Tables 1–5 the following was revealed:

1. There was a satisfactory correlation between postoperative OIH and PAH clearance with a correlation coefficient of r = 0.86 (Fig. 3).

Table 2. Clearances on day 1 postoperatively in ml/min/kg body weight (series B); from Heising (1980)

Dog serial No.	Weight (kg)	OIH clearance								PAH clearance postoperative				Inulin clearance postoperative			
		preoperative				postoperative											
		total	ri.	le.	$\frac{\text{ri.} \times 100}{\text{le.}}$	total	ri.	le.	$\frac{\text{ri.} \times 100}{\text{le.}}$	total	ri.	le.	$\frac{\text{ri.} \times 100}{\text{le.}}$	total	ri.	le.	$\frac{\text{ri.} \times 100}{\text{le.}}$
39	25	22.7	12.3	10.4	54	22.4	13.7	8.7	61	23.5	11.5	12.3	48	4.4	2.1	2.3	47
44	26	18.9	10.6	8.3	56	27.3	13.4	13.9	49	19.9	9.2	10.7	46	5.6	2.7	2.9	48
45	31	7.9	4.2	3.7	53	14.3	8.4	5.9	59	13.0	6.4	6.6	49	4.0	2.0	2.0	50
47	28	9.6	4.6	5.0	48	12.3	5.7	6.6	46	8.2	4.1	4.1	50	2.8	1.4	1.4	50
49	24	13.5	6.5	7.0	48	18.5	9.1	9.4	49	16.2	8.2	8.0	51	4.5	2.2	2.3	49
50	25	12.9	7.0	5.9	54	26.4	12.7	19.7	48	21.4	11.1	10.3	52	5.7	2.9	2.8	51
51	24	15.1	8.3	6.8	55	32.4	17.5	14.9	54	21.2	10.6	10.6	50	3.2	1.6	1.6	50
52	28	12.8	6.4	6.4	50	18.1	12.5	5.6	69	17.6	8.5	9.1	48	4.8	2.3	2.5	48
$\bar{x}$	26.4	14.2	7.5	6.7	52	21.5[a]	11.6	9.8	54.4	17.6[b]	8.7	9.0	49	4.4[c]	2.2	2.2	50
±	2.5	4.8	2.8	2.0	3.2	6.9	3.7	3.8	8.0	5.1	2.5	2.7	1.9	1.0	0.5	0.5	1.4

[a] Significantly different (raised) in comparison to preoperative total clearance of the series B, C, D as well as in comparison to postoperative OIH total clearances of series C (day 7) and D (day 28)
[b] Significantly different (raised) in comparison to (postoperative) PAH total clearances of series C (day 7) and D (day 28)
[c] Not significantly different in comparison to postoperative Inulin clearances of series C (day 7) and D (day 28)
The share of the right and lift kidneys in the total clearances at no time and with no clearance material significantly different

Table 3. Clearances on day 7 postoperatively in ml/min/kg body weight (series C); from Heising (1980)

Dog serial No.	Weight (kg)	OIH clearance								PAH clearance postoperative				Inulin clearance postoperative			
		preoperative				postoperative				total	ri.	le.	ri. x 100 / le.	total	ri.	le.	ri. x 100 / le.
		total	ri.	le.	ri. x 100 / le.	total	ri.	le.	ri. x 100 / le.								
20	22	22.2	11.1	11.1	50	21.5	8.6	12.9	40	12.0	6.1	5.9	51	5.5	2.8	2.7	51
22	28	14.7	7.5	7.2	51	9.9	4.5	5.4	45	10.8	5.3	5.5	49	3.2	1.6	1.6	50
24	33	7.3	3.9	3.4	53	13.0	6.2	6.8	48	8.8	4.2	4.6	48	2.8	1.3	1.6	46
28	28	12.6	6.4	6.2	51	14.8	7.4	7.4	50	14.4	6.7	7.7	47	4.0	1.8	2.2	45
36	27	9.4	5.5	3.9	59	8.3	4.2	4.1	51	7.7	4.0	3.7	52	2.8	1.5	2.3	54
41	23	11.8	6.8	5.0	58	8.0	4.3	3.7	54	8.5	4.4	4.1	52	1.4	0.7	0.7	50
43[a]	26	11.2	6.0	5.2	54	10.5	1.6	8.9	15	6.4[a]	[a]	6.4[a]	[a]	1.1[a]	[a]	1.1[a]	47
46	31	11.6	6.3	5.3	54	11.9	7.1	4.8	60	12.3	6.0	6.3	49	3.8	1.8	1.0	47
$\bar{x}$[b]	27.4	12.8[c]	6.8	6.0	54	12.5[d]	6.0	6.4	48	10.6[d]	5.2	5.4	49	3.4[e]	1.7	1.7	50
±[b]	4.0	4.8	2.2	2.6	3.5	4.7	1.7	3.2	6.4	2.4	1.1	1.4	2.0	1.3	0.6	0.6	3.2

[a] Postoperatively "silent kidney" right, see context
[b] Calculated without values of dog 43, see context and comment[a]
[c] Not significantly different in comparison to preoperative values of the series B and D (day) respectively day 28 postoperatively
[d] Significantly different (reduced) in comparison to the postoperative value for the series B (day/postoperatively). No significant difference in comparison to preoperative values of all series and to the postoperative value of the series D (day 28 postoperatively)
[e] Not significantly different in comparison to postoperative values of the series B and D (day/resp. 28 postoperatively)

Table 4. Clearances on day 28, postoperatively, in ml/min/kg body weight (series D); from Heising (1980)

Dog serial No.	Weight (kg)	OIH clearance								PAH clearance postoperative				Inulin clearance postoperative			
		preoperative				postoperative				total	ri.	le.	ri. x 100 / le.	total	ri.	le.	ri. x 100 / le.
		total	ri.	le.	ri. x 100 / le.	total	ri.	le.	ri. x 100 / le.								
11	28	11.6	5.7	5.9	49	11.5	4.9	5.6	43	11.8	4.8	7.0	41	3.9	1.7	2.2	44
13	27	10.6	5.5	5.1	52	7.5	3.9	3.6	52	7.1	3.7	3.4	52	2.2	1.1	1.1	50
14	25	7.3	3.1	4.2	42	7.2	3.0	4.2	42	10.4	4.7	5.7	45	3.3	1.6	1.7	48
15	24	7.1	3.0	4.1	42	7.1	2.4	4.7	34	10.9	5.4	5.5	50	4.1	2.1	2.0	51
16	26	9.1	4.4	4.7	48	14.7	7.9	6.8	54	11.1	5.6	5.5	50	4.2	2.2	2.0	52
17	24	16.5	6.1	10.4	37	14.4	7.2	7.2	50	14.7	7.2	7.5	49	3.8	2.0	1.8	53
18	28	10.8	5.7	5.1	53	8.9	5.1	3.8	57	11.0	6.0	5.0	55	5.5	3.1	2.4	56
30	33	10.3	5.9	4.4	57	11.1	8.1	3.0	73	8.1	4.3	3.8	53	2.8	1.5	1.3	54
$\bar{x}$	26.9	10.4[a]	4.9	5.5	47	10.3[b]	5.3	4.9	51	10.6[b]	5.2	5.4	49	3.7[c]	1.9	1.8	51
±	2.9	3.0	1.7	2.1	7.5	3.1	2.2	1.5	11.7	2.3	1.1	1.4	4.5	1.0	0.6	0.4	3.7

[a] Not significantly different to the corresponding preoperative values of series B and C (day 1 or day 7, postoperatively)
[b] Not significantly different to the corresponding preoperative values and to the corresponding postoperative value of series C (day 7, postoperatively), significantly different lowered in comparison to the corresponding value of series B and C (day 1, postoperatively)
[c] Not significantly different to the corresponding values of series B and C (day 1 or day 7, postoperatively)

Table 5. Series B–D, average values of the pre- and postoperative clearances[a,b]

Series/ day, post-operatively	Weight (kg)	OIH clearance[a] preoperative			OIH clearance[a] postoperative			PAH clearance[a] postoperative			Inulin clearance[a] postoperative			PAH Inulin		
		total	ri.	le.	total	ri.	le.	total	ri.	le.	total	ri.	le.	Total	ri.	le.
B/1	26.4[d]	14.2[d]	7.5	6.7	21.5[c]	11.6	9.8	17.6[c]	8.7	9.0	4.4[d]	2.2	2.2	4.00	4.00	4.00
C/7	27.0[d]	12.8[d]	6.8	6.0	12.5	6.0	6.4	10.6	5.2	5.4	3.4[d]	1.7	1.7	3.18	3.14	3.12
D/28	26.9[d]	10.4[d]	4.9	5.5	10.3	5.3	4.9	10.6	5.2	5.4	3.7[d]	1.9	1.8	2.86	2.73	2.99

a All clearance results in ml/min/kg body weight
b Distribution regarding the body side for all clearance materials and points in time not signficantly different
c Significantly raised in comparison to all preoperative OIH results and in comparison to the postoperative results of series C and D
d Not significantly different

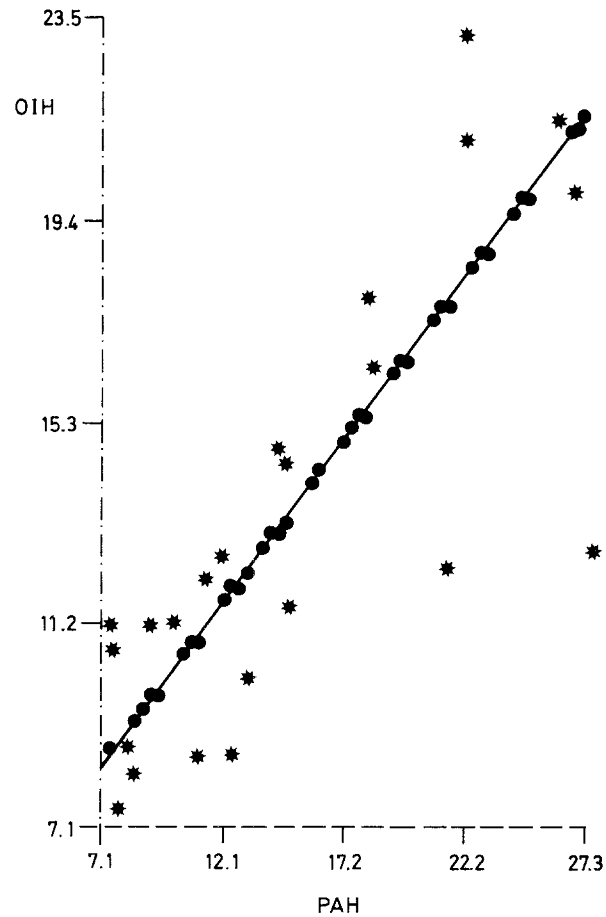

Fig. 3. Series B, C, D; correlation between postoperative *OIH* and *PAH* clearances. Correlation coefficient r = 0,86; regression line Y = A + BX with axial section A = 3,51 and rise B = 0,67. From: Heising (1980)

2. It is possible to give a qualitatively good representation of the decrease of flow by means of the parameter of the radioisotope nephrogram[7] but not quantitatively.

3. In contrast to Doppelfeld and Weißbach (1979), although in conformity with Berberich and Oberhausen (1980) we also found a satisfactory correlation between PAH and OIH clearance even in the case of upper urinary tracts obviously blocked following surgery.

4. The pre- and postoperative OIH clearance of series B (day 1 postoperatively was significantly different to $\overline{x}$ = 14.2 ± 4.8 (preoperatively or $\overline{x}$ = 21.5 ± 6.9 ml/min/kg bodyweight (postoperatively) (Table 2).

5. The length of time from the injection of the radioisotope until maximum activity (= T_{max}) is apparently physiologically shorter in dogs than in humans, thus T_{max} in two dogs amounted to 1.6 and 1.8 min, therefore the calculator programme had to be modified correspondingly in these cases.

7 Radioisotope nephrograms were carried out and evaluated for all pre- and postoperative OIH clearances. We are dispensing here with a detailed presentation and discussion.

Discussion

From clinical experience the postoperative decrease in flow was to be expected although not to the extent found (Table 1). There was a continuous increase in the flow rate postoperatively but the flow was not related to bodyweight, bodylength, preoperative OIH clearance, length of operation or anaesthesia. The findings of other authors were not available. Certainly Straube (1973) showed, using seven dogs, that following submucosal displacement of the ureter according to Lich/Gregoir method preoperative conditions of flow resumed after 10 days. However, more exact details and calculations of the significance of this are not available.

Even the radioisotope nephrograms which have not been represented here individually show that definite obstruction existed on day 1 and day 7, postoperatively. Even here the picture of a regularly appearing, pronounced decrease of flow comes to the fore despite all reservations concerning the possibility of quantifying the results of the radiosiotope nephrogram. It was no longer possible to find evidence of this on day 28 after the operation.

The postoperative clearances were not restricted at any time in any group. It is not possible to explain the raised postoperative OIH clearance on day 1 after the operation (Tables 2 and 5) in our experiments either by an increased renal cortex circulation due to obstruction [11, 14, 16] or by an intrapelvic increase in pressure [7, 9], or by an overestimation of the function of the kidney due to an increase of phase II of the radioisotope nephrogram caused by the obstruction [5; detailed discussion: 7]. Even a possible sodium induced increase in kidney function [1] could only be expected to lead to a change in the glomerular filtration rate, that means the Inulin clearance, but not to a change in the tubulo-secretory function. Because, due to the standardised experimental arrangement, diatetic considerations do not aid in interpreting these findings, it is not possible to provide an explanation based either on experimental literature nor on our own experimental arrangement. This applies in particular because this unexpectedly significant finding also affects the non-operated kidney on the contralateral side in the same way.

Acknowledgements. We are grateful to Mrs. L. Bude, E. Janz, E. Szigety, K. Uhlenbruck and Mr. D. Marosi for technical assistance and secretarial help.

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