

**Appendix I:** Summary of studies' key elements and outcomes

	<b>Schatzmann<sup>17</sup></b>	<b>Vialet<sup>18</sup></b>	<b>Ware<sup>20</sup></b>	<b>Battison<sup>19</sup></b>
Year & Country	1998, Germany	2003, France	2004, USA	2005, UK
Design	Prospective	Prospective RCT	Retrospective chart review	Prospective crossover
Subjects (% of which TBI)	6 (83%)	20 (100%)	13 (100%)	9 (66%)
Mannitol formulation	Grouped with Sorbitol	20%	Not stated, 0.25-1.9g/kg	20%
Mannitol dose	Not stated	2.3mOsm/kg	Not stated	249mOsm
Sodium formulation	10% NaCl (as rescue)	7.5% NaCl	23.4% NaCl, 30ml	7.5% NaCl + 6% Dextran
Sodium dose	Not stated	4.8mOsm/kg	240 mOsm	250mOsm
Baseline ICP: Mannitol	-	-	38	24 (IQR 18.8-25.9)
Baseline ICP: Sodium	52 ± 16	-	36	22 (IQR 20.1-26.3)
Definition of ICP control	Not stated	ICP < 25 or CPP > 70	Not stated	< 18mmHg
ICP control: Mannitol	-	3/10 (30%)	-	14/18 (78%)
ICP control: Sodium	-	9/10 (90%)	-	16/18 (89%)
Δ in ICP control	-	p<0.01 in favour of HTS	-	Not stated
ICP reduction: Mannitol	-	-	20	7.5 (IQR 5.8-11.8)
ICP reduction: Sodium	22 ± 13	-	15	13 (IQR 11.5-17.3)
Δ in ICP reduction	-	-	Not significant	p=0.014 in favour of HSD
Δ in time of onset	-	-	-	-
Δ in duration of action	-	p=0.04 in favour of HTS	p=0.016 in favour of HTS	p=0.044 in favour of HSD
Δ in CPP increase	-	Not significant	-	p=0.030 in favour of HSD
Δ in survival rates	-	Not significant	-	-
Δ in neurological outcome	-	Not significant	Not significant	-
Conclusion	HTS effective as 2nd line	HTS more effective	Both agents effective	HSD more effective

**Appendix I (continued):** Summary of studies' key elements and outcomes

	<b>Harutjunyan</b> <sup>8</sup>	<b>Francony</b> <sup>21</sup>	<b>Ichai</b> <sup>6</sup>	<b>Kerwin</b> <sup>22</sup>
Year & Country	2005, Germany	2008, France	2009, France	2009, USA
Design	Prospective RCT	Parallel RCT	Prospective open RCT	Retrospective chart review
Subjects (% of which TBI)	32 (31%)	20 (85%)	34 (100%)	22 (100%)
Mannitol formulation	15%, 1.4ml/kg	20%	20%	Not stated
Mannitol dose	Not stated	255mOsm	1.75mOsm/kg	15-75g
Sodium formulation	7.2% NaCl + HES 200/0.5	7.45% NaCl	Sodium lactate (HSL)	23.4% NaCl
Sodium dose	Not stated	255mOsm	1.65mOsm/kg	240mOsm
Baseline ICP: Mannitol	23 (IQR 19-30)	31 ± 6	Not stated	28.3 ± 8.07
Baseline ICP: Sodium	22 (IQR 19-31)	27 ± 3	Not stated	30.7 ± 7.94
Definition of ICP control	< 15mmHg	20% drop	< 20mmHg or 5mmHg drop	5mmHg drop
ICP control: Mannitol	49/53 (92.5%)	10/10 (100%)	19/27 (70.4%)	75/102 (73.5%)
ICP control: Sodium	55/57 (96.5%)	9/10 (90%)	28/31 (90.4%)	100/108 (92.6%)
Δ in ICP control	Not significant	Not significant	p=0.053 in favour of HSL	p=0.0004 in favour of HTS
ICP reduction: Mannitol	t60: 11 (IQR 5-18)	t60: 14 ± 8	4	6.4 ± 6.57
ICP reduction: Sodium	t60: 14 (IQR 7-20)	t60: 10 ± 5	7	9.3 ± 7.37
Δ in ICP reduction	p<0.0001 in favour of HES	Not significant	p=0.016 in favour of HSL	p=0.0028 in favour of HTS
Δ in time of onset	p<0.0002 in favour of HES	Not significant	-	-
Δ in duration of action	-	Not significant	p=0.009 in favour of HSL	Not significant
Δ in CPP increase	p<0.05 in favour of HES	p<0.05 in favour of MTL	p<0.001 in favour of HSL	Not stated
Δ in survival rates	Not significant	-	-	-
Δ in neurological outcome	-	-	Not stated	-
Conclusion	HES more effective	Both agents effective	HSL more effective	HTS more effective

**Appendix I (continued):** Summary of studies' key elements and outcomes

	<b>Oddo</b> <sup>23</sup>	<b>Polushin</b> <sup>16</sup>	<b>Sakellaridis</b> <sup>24</sup>	<b>Cottenceau</b> <sup>15</sup>
Year & Country	2009, USA	2009, Russia	2011, Greece	2011, France & Israel
Design	Retrospective cohort	Multicenter RCT	Retrospective	Prospective RCT
Subjects (% of which TBI)	12 (100%)	25 (60%)	29 (100%)	47 (100%)
Mannitol formulation	25%	15%, 0.5-1.0g/kg	20%, 2ml/kg	20%, 4ml/kg
Mannitol dose	412mOsm	1132mOsm/kg	Equimolar	Equiosmolar, not stated
Sodium formulation	7.5% NaCl (as rescue)	10% NaCl, 2-4ml/kg	15% NaCl, 0.42ml/kg	7.5% NaCl, 2ml/kg
Sodium dose	641mOsm	3400mOsm/kg	Equimolar	Equiosmolar, not stated
Baseline ICP: Mannitol	29 ± 8	30 ± 6	Not stated	16.3 ± 9.3
Baseline ICP: Sodium	27 ± 8	29 ± 8	Not stated	17.9 ± 9.9
Definition of ICP control	< 20mmHg	< 20mmHg	< 20mmHg	< 20mmHg
ICP control: Mannitol	-	-	-	8.4 ± 5.9hrs > 20mmHg
ICP control: Sodium	-	-	-	11.1 ± 7.9hrs > 20mmHg
Δ in ICP control	-	Not significant	-	Not significant
ICP reduction: Mannitol	t60: 6 ± 12	t30: 13 ± 7	7.96 ± 5.79	t30: 5.8 ± 2.5
ICP reduction: Sodium	t60: 12 ± 6	t30: 14 ± 5	8.43 ± 6.65	t30: 5.7 ± 3.8
Δ in ICP reduction	p<0.001 in favour of HTS	Not significant	Not significant	Not significant
Δ in time of onset	-	Not significant	-	Not significant
Δ in duration of action	-	Not significant	Not significant	Not significant
Δ in CPP increase	p=0.05 in favour of HTS	Not significant	-	Not significant
Δ in CBF increase	-	-	-	t30: p<0.01 in favour HTS
Δ in neurological outcome	-	-	Not stated	p=0.066 in favour of MTL
Conclusion	HTS more effective	No Δ; HES most effective	Both agents effective	Both agents effective

